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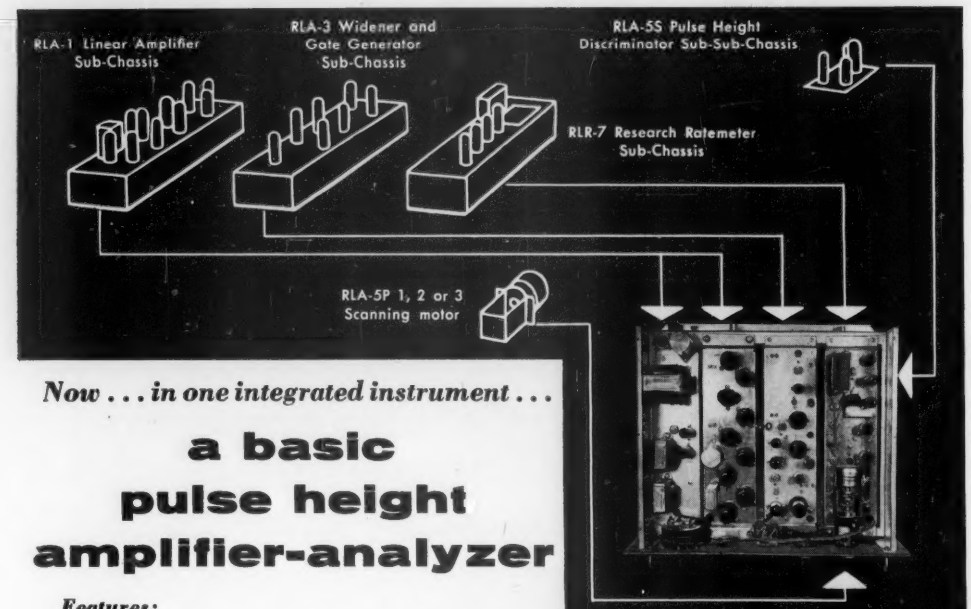

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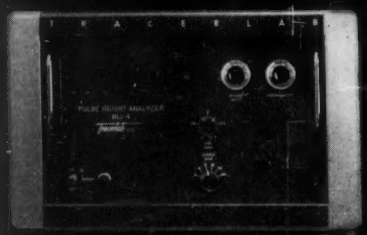

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Wish You Were Here

It takes more than a casual stopover in the magnificent new AAAS headquarters building to know your association. If each member could enjoy the privilege, as I did, of working with the staff, the board of directors, and others engaged in the association's varied activities, his appreciation of AAAS and his loyalty to it would be greatly enhanced.

Individual members may not have paused to reflect on the difficulties involved in the services performed by an organization which must somehow satisfy a diversity of specialized interests within the larger framework of all the sciences. If they could see the program as a whole, they would realize that it is far more than a compromise of special interests; it is a sound, effectively functioning unit.

The program is evolving, and the rate of desirable mutations has been appreciably accelerated during the 4 years I have been in a position to see them occur. A brief review will show not only changes but trends.

The expanded efforts of the AAAS in the field of science education are probably of greatest importance. The Science Teaching Improvement Program has already made a contribution—in less than a year—to the improvement of science teaching and the recruiting of more high-school teachers. The trial year for the Traveling Science Libraries for Small High Schools ended with reports showing enough influence on young people to justify planning for its continuance. The issuing of a recommended list of books this year should give real impetus to a movement for making scientific reading material of general interest and high quality available to high-school and college students. A new kind of Junior Scientists Assembly at our annual meetings has proved to be a promising innovation. Youth in the area where the meeting is held have an opportunity to meet and hear leading scientists, watch interesting demonstrations, and participate in panel discussions.

The symposium volume series has been modernized in format and has been placed on a more efficient and sound financial basis—without appreciable increases in book prices. More important, the methods for careful development and critical appraisal of the content of the volumes have been thoroughly reorganized.

Finally, during my tenure, the AAAS entered the field of international meetings with the successful direction of the International Arid Lands Meetings in New Mexico in 1955. It is hoped that additional interdisciplinary sessions of this kind can be conducted in the future—perhaps one on marine science, for example.

Among other avenues of service being actively explored is the education of the public about science—its aims, methods, and its basic principles. The development of this program, because of its complexity, requires careful planning and adequate financing. Plans for a series of popular science books are well advanced and will represent an initial step in this field.

The news has been getting around. Membership in the AAAS, after a static period, has started upward again. I regret that I shall now be watching future progress from the sidelines.—JOHN A. BEHNKE, *Associate Administrative Secretary*

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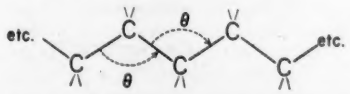
SCIENCE

Role of Crystallization in Polymers and Proteins

Paul J. Flory

High polymeric structure confers on a substance a set of physical properties which combine the capacity for long-range deformation with high strength. This unique combination of properties is unknown among other types of molecular organization. The distinguishing feature of the polymer molecule brought to prominence by attempts to establish interpretations of these properties is its remarkable configurational versatility. The possibility of rotations about the valence bonds that join successive atoms of the polymer chain gives rise to a vast array of molecular configurations. This fact assumes more than passing interest when it is realized that molecular configurations and macroscopic dimensions of a polymeric substance frequently may be interrelated. Before proceeding with the discussion of mechanical and elastic properties of polymers from this point of view, it is appropriate to consider briefly the configurational character of the long-chain polymer molecule.

A chain of $n + 1$ carbon atoms connected in series by n single valence bonds, each of length l and at an angle θ to its predecessor, is conveniently represented as follows, within the restrictions imposed by the two-dimensionality of the printed page



While this manner of representation is satisfactory for the purpose of conveying the chemical structure, it is a grossly erroneous portrayal, in general, of the spatial configuration of the chain. Rotations about chain bonds, the angle θ between successive bonds being preserved, destroy the planarity of the configuration implied by the foregoing representation. An almost unlimited variety of three-dimensional configurations differing in the values of the angles of rotation about each bond is thus possible. This multitude of irregularly coiled configurations must be summarized in statistical terms if progress beyond this point is to be made.

It is customary for this purpose to adopt the distance r separating the ends of the chain as a suitable measure of the spatial "size" of a given configuration. The planar configuration depicted in the previous paragraph corresponds to the maximum extension of the chain consistent with fixed values of l and θ. We thus have

$$r_{max.} = nl \sin (\theta/2) \qquad (1)$$

for the distance of separation of the end units in this form. In the irregularly coiled forms, such as those that arise from rotations about bond angles as discussed in the previous paragraph, the value of r varies widely from one configuration to another; generally $r << r_{max.}$ for such configurations. The average size of the polymer molecules may then be characterized by the root-mean-square value of r, which we designate by $(\overline{r^2})^{\frac{1}{2}}$, averaged over all configurations.

Theoretical calculation of the average distance between chain ends for the randomly coiled molecule recalls the classical problem of random flights treated by Lord Rayleigh, and encountered also in the diffusion of particles that are subject only to Brownian motion. In complete analogy with the displacement of a diffusing particle after tracing a path of specified length (nl), one finds that the root-mean-square of r should be proportional to $n^{\frac{1}{2}}$. If θ equals the tetrahedral angle 109.5° and rotation about valence bonds is completely unrestricted, it is found that

$$\sqrt{\overline{r^2}} = \sqrt{2}\, l \sqrt{n} \qquad (2)$$

Hence, the ratio of the root-mean-square of r to $r_{max.}$ should approximate $1/n^{\frac{1}{2}}$; if the chain is very long, the average distance r should therefore be only a small fraction of $r_{max.}$

Experiments on dilute solutions of polymers, on the whole, bear out these predictions. A polystyrene of molecular weight 1 million, for example, for which $n \cong 2 \times 10^4$, exhibits an experimentally determined end-to-end distance of about 700 angstrom units (after correction for effects of solvent-polymer interaction) (*1*). At full extension, we calculate $r_{max.} = 24{,}000$ angstroms, and for free rotation, $(\overline{r^2})^{\frac{1}{2}} = 300$ angstroms. The observed value is much closer to the latter figure, though significantly larger than it. This discrepancy is attributable to steric hindrance of rotation about the valence bonds. Configurations of most other linear polymers correlate fairly well with those calculated for a random coil. The molecules of cellulose derivatives, however, are considerably more extended, indicating a characteristic stiffness of the chain. More striking departures from the random coil configuration are found in the case of proteins such as collagen and in some synthetic polypeptides as well. Mounting evidence (*2–5*) seems to indicate persistence of rodlike, helical configurations of molecules of these substances in certain solvents even at high dilution. We shall dwell later on the consequences of this peculiarity of the protein molecular chain.

Amorphous and Crystalline States

In the bulk polymer, in contrast to the dilute solution, the chain molecules are obliged to coexist in close proximity.

The author is professor of chemistry at Cornell University. This article is based on the Harrison E. Howe memorial lecture delivered by Dr. Flory before the Rochester Section of the American Chemical Society, Rochester, N. Y., 19 Nov. 1955.

Their geometrical requirements and configurational habits must be reconciled accordingly with the limited space available. Two distinct states of the bulk polymer are clearly distinguishable: (i) the amorphous state in which the polymer chains are irregularly coiled and (ii) the crystalline state in which the chains are arranged to lie parallel to one another. If the molecules are sufficiently flexible, they may readily assert their proclivity for configurational disorder by adopting the former state. Each individual molecule in the amorphous polymer will be entangled in an utterly haphazard fashion with its many neighbors, whose configurations are similarly disordered. Indeed, it may be shown, subject to the foregoing condition of sufficient flexibility, that the configurations of individual chain molecules in the amorphous state should be equivalent to those which they would adopt in a dilute solution (*6*) (aside from effects specifically dependent on the interaction with the solvent). In other words, if the life history of one molecule of the bulk amorphous polymer could be followed photographically, it would be observed to wander, in the course of time, through a series of configurations not unlike those it would assume in a dilute solution (although the rate of transformation from one form to another would be very different). The ability of a high polymer to sustain a very large deformation when in this amorphous state (that is, noncrystalline state), is an immediate consequence of the configurational potentialities of its molecules. The randomly coiled chain molecule may comply with the applied stress merely through a readjustment of bond rotation angles. Macroscopic dimensions and molecular configurations are often directly related one to the other in polymeric substances, as I shall have occasion to emphasize repeatedly in this article.

The amorphous state of random disorder requires for its existence a fairly high minimum tortuosity of the participating polymer chains (*6*). The space cannot be filled to high density with long, semirigid rods, or even with gently curving ones. If the polymer chains concerned cannot submit to the required flexibility without intolerable strain, a state of parallel order will be preferred. In this state, the molecules may be presumed to occur either as (nearly) fully extended planar zigzag chains, or in helical forms as dictated by the stereochemical requirements of their chain substituents (and in the case of proteins by intramolecular hydrogen bonding). Thus, a state of parallel order *could* arise without the aid of intermolecular forces (*6*). In actual instances where such order occurs, forces operating between the chain molecules may be expected, however, to

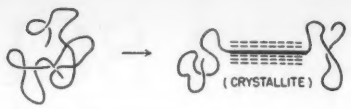


Fig. 1. Configurational change in crystallite formation.

further the ordering process. If the chain possesses a regularly repeating structure with polar groups or substituents occurring at definite intervals, such forces will tend to align adjacent chains so that polar groups and/or substituents occur in regularly spaced planes intersecting the molecular axes. We may thus construct a theoretical basis for the well-known phenomenon of crystallization in polymers. Crystallization of a polymer may therefore be attributed to two factors: chain inflexibility and intermolecular forces. The extent to which these factors are separately responsible for the crystallinity in a given polymer remains largely in the realm of conjecture and need not concern us at this point. It is sufficient to note that x-ray diffraction studies, supported by other observations, demonstrate the occurrence of states of order in polymers having structures which are repeated with regularity along the polymer chains and that in such states the chains lie parallel with their axes adjusted longitudinally as required to bring corresponding groups of adjacent chains into alignment.

Further investigations involving a variety of techniques, including infrared absorption spectra and density determinations as well as x-ray diffraction, reveal that crystalline polymers contain a proportion of polymer in the amorphous state which may comprise from 10 to 50 percent or even more of the sample. The line breadths of the comparatively diffuse wide-angle x-ray reflections are indicative, moreover, of crystalline regions, or crystallites, having dimensions only of the order of 100 angstroms. This result is supported by low-angle x-ray diffraction. The crystallites evidently are interspersed with a matrix of amorphous polymer. The crystalline regions being much smaller than the lengths of the chain molecules, each of the latter must traverse a number of the former. The participation of a portion of an irregularly coiled polymer chain in the formation of a crystallite is depicted schematically in Fig. 1.

Failure of the degree of crystallinity to rise to higher levels seems to be due to the intractability of the long polymer chain, especially when a portion of it is imbedded in a crystallite. Entangled sections of chain molecules trapped in the amorphous regions between crystallites are unable to undergo the configurational rearrangements required for deposition on the surface of a neighboring crystallite.

Crystallinity disappears above a characteristic temperature that is referred to as the melting point. Melting is accompanied by a latent volume change, a latent heat, increase in transparency (usually), and a marked decrease in elastic modulus and strength. Some investigators have nevertheless been reluctant to regard the transformation in a polymer system between crystalline and amorphous states, or its reverse, as a phase transition. This reluctance has been inspired by the submicroscopic polycrystalline structure, on the one hand, and by the rather broad melting ranges sometimes observed on the other. It may be shown, however, that the former fact does not in principle disqualify the transformation from classification as a phase transition. The breadth of the melting range may be greatly reduced by adopting a slow heating schedule which assures ample opportunity for annealing before completion of the melting process. The final disappearance of crystallinity then occurs abruptly at a reproducible temperature, provided that the chain consists of a sequence of regularly repeating identical units. This melting point is depressed by diluents in strict accord with the dictates of thermodynamic equilibrium as applied to a phase transition (*7, 8*). Crystallization of the supercooled melt proceeds by growth about nuclei which may be generated spontaneously in the pure melt or may develop about foreign heterogeneities (*9, 10*). The crystallization process conforms exceedingly well with nucleation theory of phase changes in general and hence would not be explicable as a gradual homogeneous improvement in molecular order. In the following discussion we adopt the thesis that the amorphous-crystalline transition and its reverse are properly regarded as phase transitions, notwithstanding the small dimensions of the crystallite phases.

Transformation between the amorphous and crystalline states may—under suitable circumstances, and especially at high deformation (elongation)—exert a

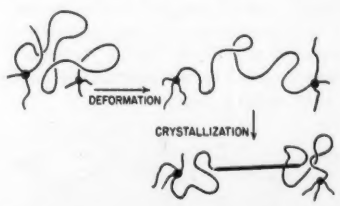


Fig. 2. Deformation of a randomly coiled chain of a network structure, followed by incorporation of part of the chain in an oriented crystallite. The crystallized portion is indicated by a heavy straight line, and cross-linked points are indicated by heavy dots.

marked effect on the elastic characteristics of the polymer. Specifically, a change in the length of the polymer may induce the development of oriented crystallites; conversely, growth of oriented crystallites may cause an increase in length. This coupling of a phase transition with macroscopic dimensional changes presents various interesting features whose importance contrasts sharply with the scant attention given to them.

Mechanism of Elastic Response in Amorphous Polymers

Let us first consider the underlying mechanism which endows a chain polymer in the amorphous state of random coiling with the capacity to translate dimensional change into stress. If we choose to characterize each random coil molecule by the vector **r** joining its ends, the lengths and directions of these vectors will vary statistically from one molecule to another. In the absence of an externally applied restraint, such as a stress which may in one way or another be transmitted to the molecules, the most probable situation for an individual molecule will be that characterized by the lowest possible value of the scalar end-to-end distance r, which will be realized when the end units of the chain lie adjacent to one another. In common with related statistical problems, however, this most probable state will be of comparatively rare occurrence owing to the competition of numerous only slightly less probable states in which the vector **r** assumes various values greater than zero though small compared with $r_{max.}$ for full extension. These deviations from the most probable $r = 0$ are statistical fluctuations, and they may be represented mathematically by the normal error, or Gaussian, function. We have already expressed the root-mean-square value of the magnitude of r in Eq. 2 for the case of a tetrahedrally bonded chain. This relationship should hold quite generally, although the numerical constant ($2\frac{1}{2}$) will need to be adjusted somewhat as required by bond angles (θ) and hindrances to rotation about them.

Owing to Brownian motions of the chain elements, the configuration of the polymer molecule will be subject to incessant rearrangements. Its end-to-end length r consequently will undergo frequent and unpredictable alterations, so that in the course of time r will wander, as it were, over the entire range of the statistical distribution. If, however, the end points of the chain were fixed in space, they would experience impulses arising from the thermally stimulated Brownian motions of the chain segments, which tend to alter the configuration. The direction of these impulses will be variable, some of them tending to increase r and others to decrease it, but averaged over a sufficient period of time their resultant will be in the direction which would, if it were permitted, change r toward its most probable value —that is, $r = 0$. The intensity of the impulses will depend on the temperature. A complete analysis of the problem shows that the average force delivered by these impulses will be proportional to the absolute temperature T and to the distance r, provided that it is less than about half of $r_{max.}$ The theoretical equation for the average force f in a single chain is

$$f = 3kTn(r/r^2_{max.}) \qquad (3)$$

where k is the Boltzmann constant, n is the number of statistical units in a chain between cross linkages, and $r_{max.}$ (see Eq. 1) is the maximum extension of the chain.

It remains to consider how the distance r of an individual chain may be coupled with the macroscopic dimensions of the sample. This will depend of course on the structure of the polymer. The cross-linked network structures, such as occur in vulcanized rubbers, are illustrative. Polymeric networks of this nature may be formed by the introduction of cross linkages at random points of contact between the randomly entangled chains of the amorphous mass. These cross linkages usually occur only at intervals of 100 or so units along a given molecule. Although intervening portions of the molecules may vary their configurations, the points of cross linkage confer a permanence on the structure such that any change of configuration (r) for one chain will entail coordinated configurational changes among those to which it is connected. If the sample is deformed, the cross linkages must assume new relative positions in space as dictated by the deformation, hence the r values for the chains running between successive cross linkages will be altered by the deformation. One may, in fact, consider the molecular chains connecting cross linkages to act like Hooke's law springs, each of which exerts a retractive force (averaged over time) which is proportional to its length r, as expressed by Eq. 3. (The actual molecular mechanism, however, is very different from that responsible for the retraction of a mechanical spring.)

When a polymer having a random network structure (for example, vulcanized rubber) is subjected to simple elongation, for example, components of the end-to-end lengths of the chains in the direction of the elongation will be increased. The resulting alteration of chain configurations produces a force tending to restore the sample to its original length. This force of retraction can thus be related to the changes in molecular configuration resulting from the deformation.

Crystallization and Dimensional Changes

Let us now examine how crystallization, under the influence of an externally applied stress, should be expected to affect the elastic behavior of a polymer. Some sort of network will again be assumed; otherwise relaxations of the chains would lead to permanent displacements of them relative to one another, and hence to nonrecoverable deformation. Consider a chain of this network situated as shown in Fig. 2 with the end-to-end vector approximately parallel to the direction of elongation produced by a fixed tensile force. It is an experimental fact that crystallites produced by stretching generally occur with chain axes rather well oriented parallel to the axis of elongation. If a portion of the chain depicted in Fig. 2 is incorporated in such a crystallite in the manner indicated, the average stress exerted by the chain at its end points will be reduced. This conclusion may be reached merely by applying the principle of LeChatelier, or from more detailed considerations as follows. The units acquired by the crystallite being relegated to fixed positions, only the residual amorphous chain units are capable of undergoing alterations of positions inspired by thermal motions; hence the retractive force is to be attributed to them only. While the remaining amorphous units are reduced in number, the distance which they must span (that is, the vector difference between **r** and the length of the crystallite) is reduced much more owing to the disproportionately greater distance taken up by those units which have crystallized. The mean degree of extension $r/r_{max.}$ for the amorphous sections will therefore have been reduced due to the nearly perfect alignment of those units which have crystallized; hence the force delivered to the cross linkages will be diminished as a result of crystallization.

Considerations such as these lead to the conclusion that orientation imposed by stretching should promote crystallization and, conversely, that crystallization in a previously oriented (for example, elongated) polymer should diminish the stress. These expectations are amply confirmed by experiments on extensible polymers that are capable of undergoing crystallization. The melting point is increased by elongation; occurrence of crystallization while the sample is held at fixed length is accompanied by a decrease in stress. If in the latter experiment the temperature is lowered below the melting point for the undeformed polymer, the stress may, during the

course of crystallization, fall to zero, and the length may subsequently increase spontaneously beyond the stretched length (*11*).

Having discussed the mechanism by which a stress is generated in an amorphous polymer as a result of deformation and how this stress may be modified by crystallization, we direct attention now to the inferences which may be drawn concerning the molecular state in a substance of unknown constitution from its elastic and thermoelastic behavior. If this substance is capable of sustaining a large elastic deformation, the presence of long, irregularly coiled polymer molecules is unequivocally indicated. If the polymer recovers its original dimensions after release of the stress, the presence of cross linkages, or physically equivalent interchain connections, may be assumed as well. Crystallization may or may not be induced during the deformation. If it is not, the deformation produces a directly calculable alteration in the statistical distribution of the lengths (r) of the chains between cross linkages. The deformed distribution will represent a less probable state and hence one of lower entropy. Assuming that the force thus generated is to be attributed solely to this change in entropy, the force at fixed sample length should *increase* directly with the absolute temperature T (see Eq. 3). If we choose to observe the length at constant force, it should *decrease* approximately (except at low elongation) as $1/T$—that is, the linear thermal expansion coefficient should be negative. Curve *a* in Fig. 3 is illustrative of this case, which applies to amorphous rubberlike polymers generally.

Consider again the elongated sample held at fixed length. If the polymer has partially crystallized following elongation, its crystallites being oriented in compliance with the deformation, the stress will have been diminished as a consequence of crystallization as previously noted. An increase in temperature will promote melting—that is, the reverse of the process depicted in Fig. 2. The release of chain units from the state of high orientation in the crystallites increases the over-all extensions of the amorphous chains. Thus, in addition to the increase in tension due to the greater Brownian motion at the higher temperature (to adopt an alternative manner of expression of the effect described in the previous paragraph), there will be a further—and probably considerably greater—increase in tension due to melting. At constant force, this will be observed as an enhanced thermal contraction, as depicted by curve *b* in Fig. 3.

Finally, if the polymer were brought to a high degree of crystallinity which remains substantially unchanged throughout the temperature interval, the material should then exhibit normal, (that is, positive), thermal expansion (see curve *c* in Fig. 3) characteristic of the crystalline state of matter generally.

The first two types of thermoelastic behavior are observed in vulcanized rubber. At moderate elongations in the range from 1.5 to 3 times the relaxed length, ideal rubber behavior (curve *a*) prevails. At somewhat higher elongations, where the rubber is partially crystalline, the melting which accompanies an increase in temperature causes the negative thermal expansion to be considerably greater in magnitude (*12*). Highly oriented fibers at temperatures well below their melting points sometimes fall in the third classification, which is better illustrated, however, by the fibrous proteins to be discussed in the second section following.

The crystal-liquid phase transition could, in principle, be used to convert thermal into mechanical energy in a heat engine in which the working substance—a crystallizing polymer—contracts at high temperatures due to melting and lengthens due to oriented crystallization as the temperature is lowered. [The Wiegand demonstration machine (*13*) is similarly actuated by the thermoelastic properties of amorphous rubber; however, crystallization probably is not involved over the range of its operation.] The elastic force and sample length in such a system would perform as analogs of the pressure and volume in a steam engine, where the phase change is one of vaporization rather than melting.

A crystallizing polymer having functional groups of such a nature as to be readily altered by a change in the chemical environment could be used as the working substance of a machine for converting chemical into mechanical energy. Alteration of the chemical environment in such a way, for example, as to promote ionization of the functional groups should encourage melting—that is, lower the melting point—and hence bring about contraction. Lengthening would be produced by an opposite change. Such a mechanical-chemical system, since it depends on a phase transition, should be a far more sensitive converter of chemical to mechanical energy than the much-discussed polyelectrolyte systems which give rise to relatively low isotropic forces of osmotic origin.

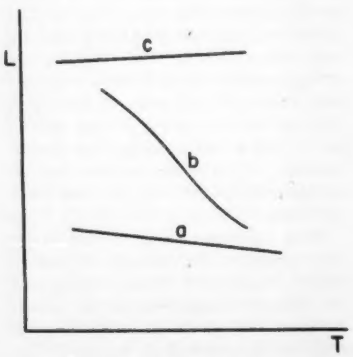


Fig. 3 Relation of length to temperature for (*a*) moderately extended ideal rubber, (*b*) oriented, partially crystalline sample, and (*c*) fully crystalline fiber.

Structure of Fibrous Proteins

Wide-angle x-ray diffraction offers abundant evidence for ordered, or crystalline, arrangements of the polypeptide chains of native proteins. The degree of crystallinity is often high, the fraction of truly amorphous, irregularly coiled chains outside crystalline regions being relatively low. On the other hand, the degree of perfection of order within the crystalline regions generally is rather low—as evidenced by the breadth and small number of x-ray reflections observed—even by comparison with the crystallinity found in other polymers. The imperfect organization of the crystalline regions probably is due to the bulkiness of the substituents on the amino acids units and to the differences between these substituents on the various peptide units.

The polypeptide chains in the fibrous proteins α-keratin, myosin, epidermin, and fibrinogen appear to be arranged in their native states in the α-helical configuration of Pauling and Corey (*14*). These configurations are stabilized by intramolecular hydrogen bonds between amide groups occurring in one turn of the helix with those of the preceding and succeeding turns. The individual polypeptide chains thus assume the forms of rigid rods having diameters (about 10 angstroms) which are small compared with their lengths. The composite fiber is made up of aggregates, or fibrils, in which the rodlike helices are aligned parallel to one another in regular (hexagonal) transverse arrangement. Intermolecular interactions between adjacent helices are weak; the structure derives its stability predominantly from the intramolecular hydrogen bonding within each chain molecule.

The configuration of the polypeptide chains in native collagen has not been established unequivocally (*15*). The N—H bonds of the amide groups, according to polarized infrared studies, are directed approximately perpendicular to the fiber axis, suggesting the possibility of intermolecular hydrogen bonding. Other evidence points to the presence of more or less discrete "protofibrillar" structural entities (*16*) consisting of either a single chain wound in a shallow helix, or of three chains wound together

in a triple helix (*15*), or possibly a "coiled-coil" (*17*), of greater pitch. Whatever the structure of the protofibrillar element of collagen may be, it seems unlikely that these elements are bound together by strong hydrogen bonds; hence the primary molecular entity for present purposes may also be regarded as an internally bonded rodlike structure.

Upon stretching under suitable conditions, the α-keratins can be converted to their β forms in which the polypeptide chains are nearly fully extended and hydrogen bonding occurs between amide groups of adjacent chains. (Silk fibroin and feather keratin possess the β-structure in their native states.) The β-form resembles more closely the structures generally found for polar fiber-forming synthetic polymers, in which the crystal structure derives its stability primarily from interchain forces. Synthetic polypeptides may similarly occur in either the α or β modifications, and in some instances either form may be obtained by casting from solutions in different solvents (*18*).

A protein can be rendered noncrystalline by subjecting it to suitable conditions of solvent environment and temperature. It then dissolves or swells; in the case of a fibrous protein, it also shrinks. The most thoroughly investigated transformation of this sort is the shrinkage of collagen that occurs in water in the vicinity of 60°C or in ethylene glycol at approximately 68°C (*19*). The sample shrinks to about 20 percent of its initial length, and the x-ray diffraction pattern which is characteristic of crystalline native collagen simultaneously disappears. In the swollen, contracted state, the material exhibits typical rubberlike behavior; it is reversibly extensible, and it responds to extension with a retractive force which, for a given extension, is approximately proportional to the absolute temperature. It must be concluded that in the shrinkage of collagen the polypeptide chains abandon the ordered arrangement of the crystal for the greater configurational freedom offered by the random coil state.

The shrinkage process in collagen occurs abruptly within a temperature interval of a few degrees, and it is accompanied by an increase in total volume, by the absorption of a latent heat, and, as mentioned previously, by a "latent-length" change. Under appropriate conditions, the melting point can be determined within a degree or two. It is increased by tensile stress and depressed by diluents in a systematic fashion. It has been shown recently (*19*) that collagen, previously rendered amorphous by heating in ethylene glycol and subsequently allowed to remain for a period of hours at a temperature some 20° below the initial melting point, gradually undergoes a spontaneous recrystallization as indicated by an unmistakable, though small, decrease in volume. When the temperature is raised, the re-formed crystalline material melts at the same temperature as previously observed for initial melting.

The array of evidence cited admits of no other interpretation than that which attributes the shrinkage of collagen to a phase transition. Nearly two decades ago, Wöhlisch (*20, 21*) applied the term *melting* to the shrinkage of collagen and published a series of papers upholding this view not only for collagen but for other fibrous proteins as well. His pioneering work has been largely ignored in recent reviews of the subject, and few investigators have pursued his ideas further. [See, however, the work of Wiederhorn and coworkers (*22*), who have treated shrinkage of collagen from this point of view with a considerable measure of success, and of Pryor (*22a*), who has given a similar qualitative account of dimensional changes in collagen and muscle.] No satisfactory alternative explanation for the pronounced dimensional changes in fibrous proteins has been offered. Whereas crystallinity in proteins has been extensively investigated, the possibility that this crystalline order should, under suitable conditions, be susceptible to melting does not seem to have received the attention it deserves (*15, 16*). The explanation for this surprising oversight probably lies in the general reluctance of investigators to apply principles governing phase equilibria to the melting, or dissolving, of a polymeric substance. Meanwhile, evidence has accumulated which fully justifies the contention that melting in synthetic polymers, natural rubber, and cellulose derivatives is in fact a phase transition (*8*). The melting of proteins obviously should now be treated from the same point of view. In so doing, we shall circumvent the perfunctory classification of the phenomenon of shrinkage in collagen and other fibrous proteins as a denaturation—a nebulous term meaning many things, but more often than not it may well be taken to signify melting.

Lack of strong interchain forces between adjacent molecules in the internally hydrogen-bonded helical form might seem to weigh against the case for a phase transition. This supposition is incorrect, however. As we have seen, melting (to be distinguished from dissolving *without* disruption of the helix) in fibrous proteins involves conversion of the polymer chains to the random coil state. Such processes must necessarily be cooperative in nature; hence they should exhibit the characteristics of a phase transition. One may, in fact, show that transformation to this random state should manifest itself as a first-order transition even if interchain forces contributed not at all to the stability of the crystal (*6*). The helical structure confers a rigidity on the molecule which dictates parallel arrangement of the molecules except at very low protein concentrations. The transition should be cooperative and of the first order, regardless of whether stabilization of the crystalline form depends primarily on intermolecular or on intramolecular forces (*6*). Moreover, even if molecularly dispersed at high dilution, transformation of a polypeptide chain from the internally hydrogen-bonded helical configuration to a random coil should occur within a narrow temperature interval, which would become vanishingly small if the chain length were increased indefinitely while maintaining constancy of composition and structure. This conclusion follows at once from considerations, which were presented recently by Schellman (*23*), of the internal energy and entropy changes associated with the transformation of individual polypeptide chains.

Recent investigations on solutions of collagen (*4, 5, 24, 25*), gelatin (*3*), and several synthetic polypeptides as well (*5*) indicate that particles of rodlike form may persist in certain solvent media, even at very low concentrations where molecular dispersion should prevail. Evidence for this conclusion rests primarily on the high viscosities of such solutions, on dimensions indicated by light-scattering measurements, and on optical rotation. Such behavior is, of course, consistent with the predominantly intramolecular character of the forces responsible for stabilization of the helical molecular configuration. Statistical mechanical considerations of the properties of solutions of highly asymmetric rodlike particles show that only a very small lateral attraction between the particles should suffice to bring about parallel aggregation of the rods (*6*).

Electron-microscope observations on fibrous proteins such as collagen, elastin, and myosin reveal the presence of fibrils having diameters down to about 100 angstroms or less. These fibrils in turn aggregate to larger filaments. The foregoing considerations suggest a mechanism of fibrogenesis involving primary formation of single molecules (protofibrils, *16*) in the rodlike helical form, which then, depending sensitively on the effect of the surrounding solvent medium on the intermolecular interaction, may aggregate to fibrils. It thus seems likely that ordered arrangement of the individual molecules precedes aggregation.

The process of formation of ordered molecular arrangements—that is, fibrils—in proteins evidently departs significantly from the corresponding generation in synthetic polymers of ordered regions—that is, crystallites. Intermolecular forces usually are assumed to contribute

substantially to the latter process (although their importance probably has been overemphasized, *6*). Successive units of the molecular chains consequently adopt the ordered configuration required for the crystalline state concurrently with, and not prior to, their deposition on the growing crystallite. The molecule as a whole, or large sections thereof, ordinarily will not assume the rodlike configuration without the incentive offered by interchain forces prevailing in the crystalline arrangement. Ordering of the molecular chains may therefore be looked upon as a consequence of crystallization. In the formation of fibrillar proteins, on the other hand, the intraparticle forces operating within the helical configuration may be sufficient alone to produce the ordered molecular configuration. Very small intermolecular attractions should then fulfill the conditions necessary for the generation of crystalline fibrillar material. Regardless of whether or not independent particles in the rodlike configuration occur as actual intermediates which subsequently aggregate to fibrils, the occurrence of crystalline order in fibrous proteins may thus be attributed predominantly to the propensity of the polypeptide chain for its characteristic rodlike helical form. It may be significant also that fibrogenesis of proteins takes place in media of very low protein concentration, whereas synthetic fibers crystallize from a concentrated solution or melt.

There is ample evidence for the formation of microfibrillar structural organization also in highly drawn synthetic fibers (*26*). However, a considerable fraction of amorphous material usually remains interspersed with the oriented crystallites, and the extent of fibrillar development appears to be much inferior to that occurring in the fibrous proteins. Irrespective of the adequacy of the foregoing interpretation, the effect of the characteristic morphology of the protein fiber on its physical properties should not be obscured by attempts to draw close analogies with synthetic polymers (other than the synthetic polypeptides, of course) and rubber (*21, 27, 28*). It may readily be shown that theories of elasticity and swelling developed for more random systems should not be directly applicable to fibrous proteins, for example (*29*). Accordingly, it becomes necessary to adapt current theories of polymer behavior to the circumstances prevailing in fibrous proteins.

Elastic Properties of Fibrous Proteins

The partial melting of a fibril consisting of a parallel bundle of polypeptide chains is diagramed in Fig. 4. In accordance with the concept of the transformation as a phase transition, the crystalline regions, or zones, are depicted as remaining highly ordered, though coexisting with an amorphous zone wherein crystalline order has disappeared altogether. The latter should therefore be rubberlike and readily extensible under tension. It is possible to show that for any tension which the amorphous fibril is likely to withstand without rupture, its length will be less than that for either the α or the γ helix of Pauling and Corey (*14*). The fibril length must decrease, therefore, as melting proceeds.

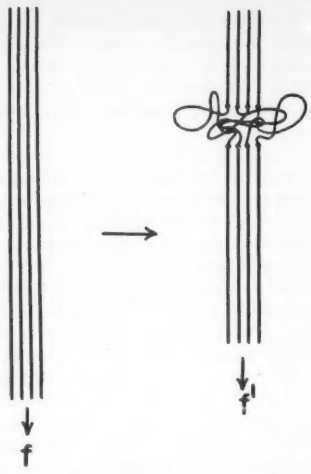


Fig. 4. Partial melting of a highly oriented fibril brought about either by elevation of the temperature or by diminishing the tensile force from f to $f' < f$.

We pause at this point to consider the force-length relation for the amorphous zone in a partially melted fibril. The configuration of the section of a molecular chain which extends through this zone will be constrained by the adjoining crystalline regions, which fix the positions of its ends. The crystalline boundaries perform the role of cross linkages in a network structure. The analogy is by no means exact, and grave errors might result if one were to adopt the tempting conclusion that conventional rubber elasticity theory should apply literally to the amorphous zone.

An important distinction arises owing to the axial orientation of the end-to-end vectors **r** for the chains which traverse the amorphous zone. Since we assume perfect parallel order of polymer molecules in the initial crystalline fibril, and since partial melting of a section of the fibril does not dislodge the bounding units, these must necessarily define a vector which is parallel to the fiber axis. (If the fibril melts completely, yet the molecules are constrained by cross linkages of one sort or another, the same considerations should apply approximately, provided that the cross linkages are separated on the average by distances large compared with the fibril diameter.) This situation contrasts sharply with that existing in a random network structure whose chain vectors are distributed uniformly over all directions in the relaxed state.

The elastic retractive force generated from elongation of the amorphous zone of the fibril should, under the circumstances described, be given merely by the sum of the forces for each of the σ chains making up the cross section, or, according to Eq. 3, by

$$f = 3kT\sigma nr/r^2_{max}. \qquad (4)$$

where n is the number of statistical segments within the length of the amorphous section of one chain, r is the axial length of the amorphous zone of the fibril, and r_{max} is its length at full extension of the chains. Equation 4 predicts a retractive force proportional to the length. It also predicts that the length of the amorphous zone should vanish under a load of zero. Imperfections of order, disregarded under the foregoing idealized assumptions, should produce (small) transverse components in the vectors **r**, and these will mitigate the physically unpalatable prediction of complete collapse in the axial dimension. Extraneous structural matter restraining transverse expansion of the fiber would act likewise. Although vitiated somewhat on these accounts, Eq. 4 may be adopted as an approximate "equation of state"; it differs from, and is simpler than, that for a random rubberlike network (*7*).

If permanent (that is, covalent) cross linkages occur between substituents belonging to adjacent chains of the protein fibril, these may be presumed to have been formed subsequent to generation of the fibril. The cross linkages are therefore superimposed on a previously ordered structure, in contrast to the conventional cross-linking of more or less randomly disordered polymer chains. Cross-linking should produce effects which are strikingly different in the two cases. Those introduced in the random state increase the modulus of elasticity in direct proportion to their number, and they diminish the stability of subsequently developed crystallites. Cross-linking of parallel chains, on the other hand, should increase the stability of crystallites (that is, raise their melting point) and have no effect on the modulus of elasticity of the amorphous polymer obtained by melting. This somewhat surprising result follows rigorously from the requirement that the end-to-end vectors for each chain lie parallel to the fiber axis (*29*). The assumed absolute parallelism will be justified only to the extent that cross-linking is confined to perfectly

ordered fibrils in which the length of a cross linkage is negligible compared with the distance between cross linkages. The qualification should not be serious, hence Eq. 4 may be expected to serve as a satisfactory approximation for the retractive force in the amorphous polymer irrespective of the degree of cross-linking.

If the fibril is uniform throughout its length, melting should take place at a sharply defined temperature which will depend on the environment (that is, the surrounding liquid medium) and on the force f. At a temperature such that the fibril is amorphous at $f = 0$, the length L should first increase continuously with f until the critical force for crystallization is reached, whereupon the sample should elongate at constant f until it is totally crystalline. This behavior, illustrated in Fig. 5, is analogous to vapor-liquid condensation, with f and L replacing P and V as variables. The value of the critical force will of course depend on the temperature and may in fact be negative.

The dependence of the length on the temperature at constant force is illustrated in the right-hand diagram of Fig. 5. At high elongations, the small positive thermal expansion characteristic of a crystalline solid is indicated. This line is interrupted by sudden shrinkage at the melting point; thereafter, the length decreases gradually with temperature as for an ideal rubber (see Fig. 3). The melting point appears as a discontinuity in the diagram and should increase with the force f. The thermal behavior of collagen in the vicinity of its shrinkage temperature conforms remarkably well to this rather idealized scheme.

Melting seems to occur over an appreciably wider range of temperature in other fibrous proteins. Such diffuse melting may be due to variations in chemical structure along the fiber axis, or to nonuniformities in the cross-sectional area. These variations should broaden the melting range, with the result that the discontinuities indicated in Fig. 5 are smoothed to continuous curves. Force-length and length-temperature diagrams for such a fiber are indicated schematically in Fig. 6. Thermoelastic behavior of the type indicated has been found experimentally for myosin (*21, 28*), collagen (*20, 21*), elastin (*30*), and keratin

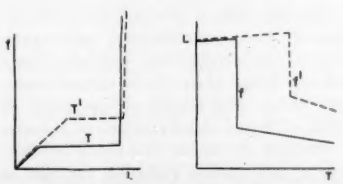


Fig. 5. Force-length and length-temperature relations for an ideal homogeneous fibril, $T' > T$ and $f' > f$.

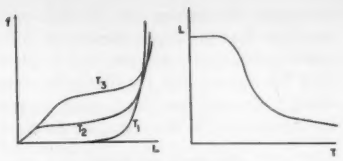


Fig. 6. Force-length and length-temperature diagrams for an inhomogeneous fibril, $T_3 > T_2 > T_1$.

(*31*). (Usually the force-temperature coefficient, rather than the length-temperature coefficient, is reported. These two coefficients are, however, directly related, though of opposite sign.) The thermal expansion coefficients are moderately negative (that is, rubberlike) for the highly shrunken fibers, strongly negative at intermediate lengths, and positive (that is, "normal") at high extensions (*27*). No adequate explanation has heretofore been given for this peculiar pattern of thermoelastic behavior. The wide variation of the thermoelastic coefficient over the extension range has led some writers to discount altogether the significance of thermoelastic measurements on protein fibers (*32*); others have drawn conflicting conclusions arising from differences in the state of the fiber under the experimental conditions (*33*). The superficially peculiar changes exhibited by the thermoelastic coefficients find straightforward explanation in the hypothesis of a phase change.

The stress-strain curve for resting muscle (*34*) shown in Fig. 7, corresponds approximately to the curve for T_1 in Fig. 6. Even at a force of zero, under the particular conditions involved, the fiber is predominantly crystalline, although a substantial portion of it may be presumed to be amorphous. With further elongation, the stress-strain curve turns rapidly upwards, and the differential elastic modulus approaches the high value characteristic of complete crystallinity. Virtual elimination of rubberlike elastic elements at the highest elongations attainable is indicated by reversal of the sign of the thermoelastic coefficient to a positive ("normal") value (*28*).

When resting muscle (in contrast to stimulated muscle) is stretched, heat is evolved (*34*) and the volume of the system decreases slightly (*35*). The former of these observations is a thermodynamically required concomitant of the pronounced increase in stress observed with rise in temperature (*21, 28*). Both observations provide compelling evidence for crystallization upon stretching, as was recognized by the investigators responsible for the observations cited (*21, 28, 34, 35*). Whether or not the crystal-liquid transition (as here considered) is an integral part of the mechanism of dimensional change was not, however, explicitly answered (*34, 35*). Other authors have been inclined to dismiss the thermoelastic effects and indicated changes in crystallinity as matters of secondary importance.

The evidence is less clear in the case of stimulated muscle. Thermal and volume changes are actually the reverse of those cited for resting muscle, heat being evolved (*36*) and the volume decreasing (*37*) when the excised muscle, or muscle fiber, is stimulated under either isometric or isotonic conditions. These results might seem to rule out melting during contraction in active muscle. It must be borne in mind, however, that the complex chemical changes, brought on by stimulation and occurring in the muscle and in the associated sarcoplasmic fluid, may well obscure the thermal and volume effects due to partial melting of the muscle fibrils.

Absence of positive evidence notwithstanding, it is tempting to speculate that partial melting of crystalline fibrils may also provide the key to the mechanism whereby muscle transforms chemical energy to mechanical energy with such remarkable facility. On this view (see Pryor, *22a*), contraction of active muscle is due to melting brought on in some manner by stimulation; lengthening during relaxation signifies recrystallization. It remains to consider how chemical energy is brought to bear on the phase transition during the period of nonequilibrium of the muscle fiber and its environment resulting from stimulation.

Now a change in the chemical environment will, in general, alter the chemical potential of a polymer in the liquid, that is, solution, state. The melting point, or range, will be shifted by such a change. The degree of crystallinity, and hence the external dimension, will reflect this change most sensitively if the fiber is in-

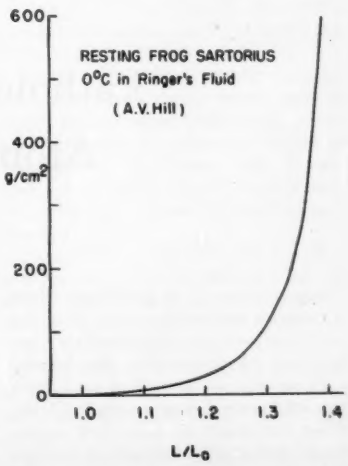


Fig. 7. Stress-strain curve for resting muscle according to A. V. Hill (*34*).

termediate in degree of crystallinity. The "razor edge" character of the dimensional change in muscle may thus be explained.

As for a more precise description of how the chemical environment may affect the crystal-liquid equilibrium, we can only surmise that a reagent generated during stimulation, and presumably a product of myosin adenosine triphosphatase activity, is operative in this connection. It may tend to form complexes with functional groups of the protein or to ionize the latter by proton transfer. One may suppose that accommodation of the complex, or of the ionic group plus its gegenion, is sterically difficult, if not impossible, within the crystalline phase, but that no corresponding difficulty arises in the liquid state. The postulated reagent should therefore tend to shift the equilibrium in favor of the amorphous state, thereby promoting shortening. Its dissipation should allow recrystallization during relaxation, and hence a restoration of the initial (rest) length.

The foregoing explanation seems to be free from a number of objections which may be leveled at the current view that dimensional changes in muscle are inspired by alterations of the charge on the protein molecule considered as a random coil polyelectrolyte. The "electrostatic" theory disregards the crystalline morphology of muscle and leads inevitably to the prediction of more or less isotropic changes in dimensions (that is, shrinkage and swelling, rather than contraction and elongation). It offers no satisfactory basis for the peculiar thermoelastic effects observed. Moreover, it is extremely doubtful that the forces generated in tetanic contraction could be held in abeyance by electrostatic repulsions between charges situated on the resting muscle fibril immersed in the sarcoplasmic fluid.

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Pathologic Effects of Atomic Radiation

Appreciation of the pathologic effects of radiation on man has required of this committee and its subcommittees consideration of voluminous experimental work on animals, as well as such direct data on human beings as are available. When the results of controlled experimental studies are considered in the light of the human data, it is found that the sequence of pathological changes is indeed quite similar in man and in animals, although man has certain definable peculiarities of response.

The human data include: (i) results of excessive exposure to x-rays and radium in the early days; (ii) results of more moderate exposure to different forms of radiation, as experienced by cyclotron workers; (iii) results of introduction of naturally occurring radioelements into the body, notably radium preparations and thorotrast; (iv) effects of exposure at Hiroshima and Nagasaki; (v) observations on populations irradiated by fallout; [and] (vi) additional observations from clinical radiotherapy, use of artificial isotopes in therapy, a very limited number of accidents in atomic energy work, and certain statistical surveys of large groups.

Experimental work covers the whole field and includes studies of acute and chronic effects on many species of animals.

Certain human effects have to be assumed from consideration of experimental knowledge—for example, early effects of high doses to the central nervous system and results of absorption of most of the artificially produced isotopes—and it is fair to say that the lethal dosage of penetrating radiation for man is less well known than for many other species.

Radiation has been added to the means

of production of casualties in warfare. Not only can radiation cause death or immediate or delayed injury by itself, but exposure to it intensifies the seriousness of burns or other injuries. The acute lethal dose for half of a given population is in the range of 400 to 600 roentgens.

Despite the existing gaps in our knowledge, it is abundantly clear that radiation is by far the best understood environmental hazard. The increasing contamination of the atmosphere with potential carcinogens and the widespread use of many new and powerful drugs in medicine and chemical agents in industry emphasize the need for vigilance over the entire environment. Only with regard to radiation has there been determination to minimize the risk at any cost.

It appears, however, that a fairly clear general picture of human radiation effects can be presented. Members of this group and of its subpanels, while recommending various points of departure for greater consideration and further research, were in no case of the opinion that any sort of "crash program" would be desirable or profitable.

The various means whereby persons may be overexposed to radiation will have a great deal of influence on the over-all effects. For example, the exposures at Hiroshima and Nagasaki and a few exposures in accidents in atomic energy plants involved radiation to the whole body in which the clinical effects reflected mainly injury to the blood-forming tissues and intestinal tract. These tissues are very sensitive to radiation but have a great power of recovery.

Where, on the other hand, exposure has been suffered at a relatively low level from time to time over a period of years, a variety of injurious effects may be encountered, such as leukemia and skin cancer. Among those who have adhered to present permissible dose levels, none of these effects have been detected.

Table 1. Average age at death.

Group	Age (years)
Physicians having no known contact with radiation	65.7
Specialists having some exposure to radiation (dermatologists, urologists, and so forth)	63.3
Radiologists	60.5
United States population over 25 years of age	65.6

Shortening of life span may result from exposure to radiation not only as a consequence of damage to a specific tissue, as seen in the development of skin cancer and leukemia, but also as a result of such general factors as lowered immunity, damage to connective tissue, or premature aging. Older members of the populations seem to be more sensitive to this nonspecific damage. The shortening of life correlates roughly with dose of radiation, but has not yet been demonstrated at low doses. . . . Table 1 indicates life shortening in radiologists, who may well have received doses in the course of their occupation ranging from very slight to about 1000 roentgens.

Shielding of even a portion of the body from radiation lessens the effect out of proportion to the relative amount of tissue protected. Therapeutic radiation to a single portion usually is much greater than the lethal level of total body radiation.

Radiation may have its prominent effects in particular parts of the body when it is applied locally, and this may take place in two ways. First, an external source may be so handled as to direct its radiation to a particular part; in this way many of the early radiologists suffered acute or chronic injury to the hands, which has also occurred in more recent atomic energy accidents.

In the second instance, a radioactive substance may be taken into the body and deposited where it is a source of constant local irradiation until it is eliminated. Bone disease in radium workers and lung disease in miners of radioactive ores (both leading to cancer as a late development) are well-known examples of this mode of exposure. It is worth noting that the atomic energy industry, through diligence, has apparently avoided exposures leading to this type of injury.

It is thus characteristic of the radiations that their effects may manifest themselves not only immediately, but perhaps only after a long period of intermittent radiation, or may even be long delayed after a single exposure. One of the particular tasks of the panel has been to see all of these effects in a common perspective. They are discussed here in terms of the effects of radiation on the important organs and tissues of the body, since it is a well known fact that some are more readily injured by radiation than others, and that injury to some has more serious consequences than to others.

Effect on Organs and Tissues

Among the more serious effects of radiation are those on the blood, since the vital blood-forming organs are particularly sensitive to radiation injury. The white blood cells are decreased in number soon after radiation, and in fatal cases they almost disappear before death. Other acute changes in the blood give rise to disorders in the clotting mechanism and a bleeding tendency, and the formation of antibodies against infections is impaired. These changes lead to acute illness in the second week (perhaps a little later in man), heralded by decrease in the white cells.

In the next few weeks anemias may occur due to deficiencies in red blood-cell formation and survival. Those victims living through the first month usually recover, but in certain individuals, or where radiation is continued, there is a further serious breakdown of blood-cell formation.

Some late effects of radiation appear as leukemias, which are found to arise a few years after radiation. This disease, relatively rare in man, may show manifold increase in persons subjected to a nearly fatal single dose (Hiroshima data) or in those whose professional work has exposed them to higher than acceptable permissible dose rates.

Effects on the intestinal tract are also critical in the early period. Vomiting and diarrhea occur within a few hours. This is a common complication of x-ray treatment to the abdomen, but is not fatal. It seems to be mediated through the vegetative nervous system and is probably not related to later damage.

Within a few days (usually 4 or 5) after radiation, more serious effects occur. Failure of the cells lining the intestine to replace themselves results in denudation of the surface, with intractable loss of fluid and salts, complicated by ulcerations, spread of infection, and bleeding.

Late effects are seen after heavy radiation therapy and resemble those seen in some other heavily irradiated tissues: overgrowth of connective tissue (fibrosis) and decrease in the number of functioning epithelial cells. Cancer has occurred in animals given overwhelmingly large doses of isotopes in insoluble form by mouth.

Effects of radiation on skin have been widely observed. On the first day an erythema, resmbling that of sunburn, ap-

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pears but is transitory. A few days later a somewhat more persistent erythema occurs which may be associated with pigmentation. Ulceration may occur in this period after high doses. Much later, atrophic changes are seen, with marked deficiency of the blood supply and intractable ulceration; such a chronically damaged skin is a fertile bed for cancer development. The Marshall Island group, while receiving total body radiation insufficient to produce serious changes, had rather marked secondary skin lesions from direct contact with fallout material. Slight local vascular changes have been observed after 2 years, but serious aftereffects are not anticipated. Falling of hair was temporary in these persons; heavy dosages are required to make it permanent. In animals, destruction of the pigment cells causes regrown hair to be white, but such loss of pigment seems not to take place in men under comparable conditions.

Bone: Early radiation effects are not of note, except that retardation of growth of epiphyses of immature bones occurs and may produce serious results in children given local radiation therapy. Late effects are seen in radium poisoning, where we see repeated destruction and repair, culminating in widespread destructive changes in which bone sarcoma is likely to appear.

Lung: Early after large doses we see congestion and increased secretion. Here, again, the late-appearing changes are of greatest importance: fibrosis, and development of cancer, which has been very common in mining areas where large concentrations of radon gas were inhaled.

Thyroid: An early and persistent effect is depression in secretory activity, which is used as the basis of the radioiodine therapy of hyperthyroidism. No serious late local effects of thyroid radiation in adults have been recorded, although some leukemias have followed heavy radioiodine treatment. A small proportion of children treated with x-ray to the upper part of the body, however, develop thyroid cancer later on, suggesting an especially high sensitivity of the child's thyroid.

Eye: The only noteworthy lesion is cataract of the lens, which is a late response. It is much more readily produced by neutrons than by x-rays [and] therefore has been most prominently observed in cyclotron workers.

Gonads: A single sublethal radiation dose to a male may result in sterility after 2 to 3 weeks, followed by a slow recovery. Chronic treatment results in a gradual reduction in number, motility, and viability of sperm. This is the most sensitive indicator of chronic damage so far observed, being measurable in dogs at 10 times the permissible dose rate. Larger doses (about equal to the total-body lethal dose) permanently sterilize males and females. Experience with the Marshall Islanders, the exposed Japanese, and certain accident cases indicate that total body doses up to about 40 to 50 percent of the lethal one have no permanent effect on human fertility.

Central nervous system: observations in man are quite limited. Very high doses given to animals result in loss of coordination and excitement soon after irradiation. At later stages, various effects are seen which indicate sensitivity of particular cells and areas.

Effects on embryos: treatment of embryos at various stages of development may lead to highly specific malformations depending on the exact developmental stage at the time of irradiation. At critical stages, relatively low dosages (those permitting survival of the mother) may cause serious malformations. These changes must be distinguished from genetic mutations, as one is often tempted to call abnormal offspring mutations. The type of malformation discussed here would not perpetuate itself genetically but would result from radiation during gestation.

It must also be remembered that there are various other agents causing malformations during development, of which German measles is a well-known example.

Factors Influencing Sensitivity

A few factors influencing sensitivity might be mentioned. Very young or very old animals have increased sensitivity to lethal effects. Growing tissues are generally more readily damaged. States like hibernation delay the appearance of radiation damage but do not prevent it. Moderate stresses do not seem to effect sensitivity, but severe ones such as burns or exhausting exercise have a deleterious influence, augmenting sensitivity.

Local radiation in sufficient amount to almost any part of the body may produce cancer, the chance of tumor development being somewhat related to dose. Since the cancer cell is an altered type of a normal tissue cell, it has often been suggested that cancer is a somatic mutation, like a genetic mutation but arising in a tissue cell which perpetuates the character by its growth.

All types of induced and spontaneous tumors appear not to arise at once, but to pass through a series of preliminary stages; and radiation-induced tumors take a particularly long time to develop. Radiation-induced cancer occurs in the absence of a generally abnormal state of the tissue of origin. Mouse experiments show that shielding of a part of the body will prevent radiation leukemia and that shielding of one ovary will prevent a tumor from developing in the other; and several of the tumors appearing late after irradiation seem to be produced in response to indirect mechanisms. If somatic mutation is a necessary part of the induction of cancer, it would seem to play a minor role.

Small Dosages and Large Populations

We have so far considered effects of overdosage of radiation in various forms. The question must necessarily be considered whether much smaller amounts of radiation, harmless to individuals, might be deleterious to large populations. Because of the striking difference between germinal and somatic cells, the former carrying on from generation to generation injuries received, the genetics committee has recommended for large populations permissible dose levels of radiation lower than those which are safe for any one generation. If the permissible dose level which they have hypothesized as desirable for large populations were to be applied, there would be no demonstrable somatic effect, although a theoretical minor shortening of life span could not be ruled out.

With regard to internal contamination, independent data on Rongelap inhabitants and Japanese fishermen indicate that a considerable proportion of the lethal dose of external radiation was received by individuals who barely exceeded, and only for a short period, the permissible internal burden.

The only situation worth considering in relation to large-scale pathologic effects would then be widespread contamination with strontium-90, which is a long-lived (half-life 10,000 days) readily absorbed, bone-seeking isotope which tends to fall out generally over the earth rather than in accordance with the usual close or intermediate fallout pattern. It has already been found that some young individuals have retained 0.001 microcuries or one-thousandth of the permissible dose. This amount if maintained through life would yield 0.2 rep (equivalent roentgen) to the skeleton.

In developing an unequivocally safe amount, we can recall that a certain degree of radiation exposure has always been with us, even excluding x-rays, in the form of gamma radiation from minerals, cosmic rays, and radioelements normally in the body. These levels vary greatly from one location or altitude to another and are not considered to produce harmful effects.

There seems no reason to hesitate to allow a universal human strontium (very similar chemically to calcium) burden of one-tenth of the permissible, yielding 20 rep in a lifetime, since this dose falls

close to the range of values for natural radiation background. Visible changes in the skeleton have been reported only after hundreds of rep were accumulated and tumors only after 1500 or more [were accumulated].

In relation to world-wide contamination, food chains are important. Fallout contaminates plants through ground and leaf deposition; animals eat these plants. Therefore, milk and cheese are human sources of radiostrontium, being high in calcium. Throughout this chain, strontium is discriminated against relative to calcium, which reduces the hazard somewhat. It must be remembered that in regions where soil and water are low in calcium, calcium and strontium will be more readily taken up.

Therapy of radiation injury: while treatment is difficult, some success has been achieved with antibiotics and properly timed blood transfusions. Shielding of a portion of the body appears to give a degree of protection disproportionately large for the mass shielded. Experiments set up to explain this fact may help in developing a rational treatment. Also, various forms of treatment given immediately before radiation have been devised, but do not appear in any sense practical. Studies of this sort may, however, provide a basis for future discoveries. . . .

Agriculture, Food Supplies, and Atomic Radiation

The committee interpreted its task as requiring its members to survey the scientific aspects of that great sequence of events which precedes the delivery of food items to the ultimate consumer, and to do so from two separate viewpoints. These were (i) the beneficial effects that may result from the deliberate involvement of radiation of any sort with constructive intention, or what has been spoken of so frequently as the "peaceful uses of atomic energy," and (ii) the harmful or disadvantageous effects of radiation of any sort due to nuclear warfare, to accidents involving atomic power plants, or even to a slowly rising background of radiation that conceivably may follow as a result of atomic technological developments in industry.

Public and private funds are currently being expended in the United States for research in agriculture and food processing at a rate in the vicinity of $300 million annually. An undeterminable but not insignificant fraction of this considerable body of research involves radiation or radioistotopes. Members of the committee did not believe it to be incumbent upon them to defend or justify, to criticize, or to challenge applications of atomic radiation to agriculture that have been developed or are under discussion. They did not wish to evaluate the programs of particular agencies or groups, but instead with judicial mind to examine the accomplishments and the potentialities, the implications and the limitations of radiation as related to the production and processing of agricultural products.

One broad conclusion is that there is not imminent any drastic change in *agricultural production* as a result of the application of radiation. However, radiation techniques provide new tools for research and may aid agricultural production by improving and enhancing the efficiency of production methods.

The committee is strongly of the view that the applications of radiation will be of far greater immediate consequence to agricultural research than directly to agriculture, and that most of the benefits that may arise to agriculture, as manifest in the availability of an adequate and varied supply of wholesome food for man, wherever he may be, will come as a summation of many improvements, small and large, in materials, in plants and animals, and in the technology of husbandry and processing developed through programs in agriculture and food processing research.

Changes therefore may be expected to come in a series of little steps, none of which in themselves may be of great impact, but which, through the years, are likely to be impressive in their total.

Another broad conclusion is that the slowly rising background of radiation caused by weapons testing in peacetime at the present rate is not likely to impair or interfere with food production. Levels of radiation considered tolerable by man are below those believed to have effects in plants or animals that would place food production in jeopardy. However, the high levels of radiation which might develop in small or large areas as a result of [the use of] atomic or thermonuclear weapons in wartime, or from mishaps with nuclear power plants in peacetime, could have catastrophic effects on agricultural production that might be of long duration, because of injury to personnel and animals, disruption of services, and contamination of soil, vegetation, and water supplies.

Tracer Studies in Agriculture

In the consideration of the beneficial effects of radiation, the committee endeavored, not wholly successfully, to separate in its thinking those benefits that may arise from additions to the pool of basic knowledge about plants and animals and their welfare from those more direct effects that may specifically result from the exposure of plants, animals, or agricultural products to radiation. Tracer studies in the biological sciences have already been enormously fruitful in aiding the elucidation of essential metabolic processes in plants and animals and may be expected to be increasingly so as the number and diversity of such experiments increases. When there is knowledge and understanding of a process, then comes the opportunity to control it for a desired end; in this way the art of agriculture is transformed to the science of agriculture.

The committee endeavored to make the separation mentioned above because

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of the conviction that there is nothing unique about radioistotopic studies as applied to agricultural research. Tracer techniques, however, frequently permit answers to be obtained to questions which seemed previously unanswerable by conventional experimentation. The involvement of isotopes puts a new dimension into metabolic studies, and areas, formerly dark, may now stand out in relief.

It is worthy of comment that many of the applied problems involved in the arts or technology of agriculture are as susceptible to study by procedures involving radioisotopes as are those more basic questions of plant and animal physiology or nutrition. Excellent examples of this type of employment of isotopes are to be found in work on the placement and recovery of phosphorus fertilizers in soils, the efficiency of various methods of application of insecticides, fungicides, and herbicides, the determination of postharvest residues of such chemicals, the extent of utilization of feed components by animals, and so forth. It is to be anticipated that there will be greatly increased use of tracer radioisotopes in the solution of such applied problems and that the immediate dividends from such research may be considerable. Further, it is likely that new methods of employing isotopes advantageously will be developed; the ingenuity of investigators in this field should not be underestimated.

Because of the unanimity of their views as to the enormous potentialities of isotope tracers as a research tool in agricultural science and biology generally, the committee gave some consideration to whether there are limitations in facilities for training or funds for specialized equipment for such studies. The consensus seemed to be that motivation for the use of such techniques must come from individual investigators themselves, that the necessary know-how is to be found in almost all research institutions, and that progress in agricultural research is not at the moment limited by inadequacies in dissemination of knowledge and techniques. There was, however, a feeling that much of the graduate training in this field is rather informal, that more universities might consider establishing courses in which the methodology, techniques, and principles of this new and powerful science are expounded, and that there is an additional need for an advanced training program for specialists in radiochemistry and radiobiology who may be developers of new techniques or interpreters of new applications of potential value in agricultural research.

Crop Production

It is abundantly established that mutations can be induced in many plant species by exposure to x-radiation, gamma radiation, and other forms of radiation. The changes which result are possibly due to chromosome deletions or aberrations. There is some difference of opinion whether radiation-induced mutants intentionally obtained are qualitatively identical with those which occur spontaneously from naturally occurring mutagenic agents, but there is no doubt that their frequency is increased. Even so, the mutation rate in most species is still very small, and furthermore most mutations are disadvantageous. The investigator seeking to exploit this phenomenon must expect to have to handle very large populations, and so far he has been able to look only for desirable changes that are reflected in morphology or appearance and therefore can readily be seen, or for changes which can be recognized by some blanket method such as inoculating all irradiated plants with disease organisms in the hope of finding one or more exhibiting resistance to infection.

It is likely that characters at present unrecognized also undergo change and that there are unexplored potentialities for effecting improvement in quality that may alter the demand for the plant, or in physiological properties that may alter the relationships of the plant with its environment.

It would be a mistake to imply that this new development has greatly simplified the tasks of those involved in crop improvement. On the contrary, it has made them more complex, but, by extending the boundaries, offers many new possibilities. It is not to be expected that acceptable new agronomic varieties can be obtained by simple irradiation of present varieties, though this is possible if large enough populations are examined. In general, however, back-crossing and recombination are needed to add the new characteristic to a crop plant acceptable in other repects.

As yet relatively few new varieties of economic plants, developed from radiation-induced mutants, have actually been introduced and widely planted. These, however, do attest to the potentialities of this procedure. Much of the research effort in this field has properly been devoted to the investigation of techniques, to such vital questions as the determination of the particular stage of development at which radiation exposure may be most effective, and to the comparative mutability of crop species. It appears that different species cannot be expected to respond in an identical manner. More perhaps is known about this aspect of corn genetics than of any other major crop plant.

Mutations in microorganisms may similarly be induced by exposure to various types of radiation, though at considerably higher radiation levels than with crop plants. The changes induced have been shown to include the degree of virulence and host range of certain pathogenic fungi. The suggestion has repeatedly been made that the plant pathologist should examine this phenomenon so as to anticipate disease-resistance requirements in a breeding program. As yet, however, there have been no significant results along these lines. Considerable success has been achieved in the development of greatly enhanced antibiotic production by some molds through radiation-induced mutation and selection. Similar genetic changes in the case of other microorganisms have produced information about the likelihood of genetic control of metabolic processes.

There is considerable evidence that bud mutations or somatic mutations can be induced by radiation and that this phenomenon can be exploited in the development of new strains of crop plants that are normally propagated by cuttings and grafting. This may be of special value in the improvement of some such crops, but as yet there have been no striking accomplishments in this direction. Progress in such studies is, however, inevitably slow because of the nature of the materials and the length of time necessary to recognize a desirable change and to produce the stocks necessary for field evaluation.

Since the mutation rate of plants may be enhanced by radiation, presumably there is some possibility of the appearance of undesirable mutants in areas where the background radiation becomes higher than normal for any reason. This may be of some significance in connection with waste-disposal practices or atomic accidents. There is, however, no evidence of such changes in areas containing radioactive springs or ores. This may be due to lack of intensive examination of the vegetation of such areas, and such surveys are to be encouraged. However, the likelihood of appearance of undesirable lines under radiation levels that would be tolerated on other grounds seems small.

There is no evidence that plant growth is stimulated or crop yields increased by exposure to low levels of radiation, despite earlier well-publicized claims to this effect. Radioactive fertilizers, used in a conventional manner, produce yield increments no greater than expected from ordinary fertilizers.

Plants accumulate nutrient elements present in the root zone in solution or absorbed onto soil colloids, but nonnutrient elements are not excluded and may similarly be taken up. The availability of radioisotopes has greatly improved the understanding of plant nutrition and soil-plant relationships and may be expected to aid substantially in the improvement of cultural practices, as indicated earlier.

Through the use of isotopes it has been demonstrated unequivocally that certain elements can enter the plant through the leaves. This is of some consequence in relation to fallout. Radioisotopes of long life or high activity if deposited in fallout from an atomic or thermonuclear incident are likely to be accumulated in crop plants by root uptake from the soil and entry through the foliage. Some of the products deposited may be initially quite insoluble, but may become soluble through weathering. Others, initially soluble, may be irreversibly fixed by many soils in a form not readily available to crops. It appears at present that strontium-90 and iodine-131 are the chief radioactive elements which are of concern in such circumstances. The subsequent use of such crops presents a great diversity of problems depending on the level of radioactivity, its nature, and the specific use of the crop. The committee was interested to learn that the Department of Agriculture is preparing for farmers some informational material relating to these problems.

The committee desires to examine further the available information on the interactions of fallout components with soil, their entry and accumulation in crop plants in order to determine whether there is available the necessary basic information from which appropriate agronomic recommendations could be formulated for agricultural operations in areas that may have undergone any likely level of contamination.

Animal Production

Whereas it appears that crop improvement programs may be considerably aided by the availability of radiation-induced mutants that may have certain desirable characteristics capable of incorporation into an agronomically acceptable variety, currently available evidence does not suggest that a similar approach with animals would be so rewarding. This statement is made not from a belief that farm animals are inherently less responsive to radiation than plants, but because physical differences of size, cost, generation time, and so forth militate against extensive studies with animals and act as obstacles that cannot readily be overcome. Probably only with poultry and to a lesser degree with swine would it be possible to handle large enough populations, and even here, if one extrapolates from the smaller laboratory animals, the chances of improvement seem slim. At present, one such study, with chickens, is known to be underway.

Limited whole-body exposure studies with farm animals have primarily been carried out to investigate physiological and pathological changes, often with the intention of transferring the information by analogy to problems of responses in man. The sequence of changes induced in most farm animals by heavy radiation exposures has been well defined. There are one or two examples, however, of the use of radiation exposure as a research tool for inhibiting certain functions in animals. For example, various functions in the oviduct of poultry can be blocked by proper radiation techniques, thereby permitting a study of the contribution made by the parts of this organ.

Much of the work with radioisotopes in the animal field centers around problems of animal nutrition and metabolism, and substantial progress has been made both in the elucidation of fundamental problems of animal physiology as well as in those of a more applied character, such as the utilization of feed constituents and the incorporation in animal tissues of inorganic constituents of forages. The experimenters in this field at present encounter one serious difficulty, which in the case of the larger farm animals greatly limits the scale of activity. This is the problem of the salvage or disposal of animals after use in experiments involving radioisotopes or radiation exposure. Even in the case of short half-life isotopes and at tracer levels only, the animals cannot be marketed through the usual outlets. This problem is of course much more serious with dairy or beef cattle than with hogs or poultry because the cost to the program is so much greater. Moreover, this limitation tends to restrict undesirably the scale and scope of such experiments, with the result that the conclusions may be less surely established than if the numbers of animals used were larger.

It appeared to the committee, therefore, that essential research on farm animals using radioisotopes or radiation is being discouraged by the high costs involved because animals must be destroyed at the termination of experiments. It recommends that a special committee be appointed to study this problem and to develop procedures and standards that, if followed and enforced, would adequately protect the consumer but permit the marketing of animals that in experimentation have been brought into contact with radioactive substances or exposed to radiation.

The welfare of the livestock population is enhanced if troublesome insect pests can be controlled or eradicated. As mentioned earlier, insecticide studies have been greatly aided by the availability of radioisotopes as tracers, but in addition there may be certain opportunities for control of insect pests by taking advantage of radiation-vulnerable stages in their life cycles. Eradication of the screw-worm fly from the southeastern United States is to be attempted, based on the virtual elimination of this fly from the island of Curaçao by the release of males rendered sterile by radiation exposure. This technique may not be generally applicable to all insect pests.

Radioisotopes in Agricultural Products and Foods

The committee discussed in detail some of the difficult problems that may arise because of the presence of a radioisotope burden in agricultural products and foods higher than that "naturally occurring." The applicable legislation in this area is clouded with uncertainties because the very possibility was not envisaged by those who enacted the laws and defined the responsibilities of the agencies that protect the public food supply. There are no permissible limits for radioisotopes in foods; any burden above the "natural" is regarded as undesirable. The current interpretation of the law places isotopes in the same category as poisonous additives. It is difficult, however, to be wholly consistent in this, inasmuch as the normal radioisotope burden varies considerably in different agricultural products, and in the same product from different locations. Moreover, the testing of atomic and nuclear weapons is placing in soil, water, and air, the world over, radioisotopes not formerly present, though at extremely low levels. The "natural content" of foods now consumed by animals and man is not the same as in the preatomic age. Though extremely small, the increment is measurable and inescapable.

It is to be anticipated that there will be in the years ahead a slowly rising background of radiation manifest in agricultural and food products by the presence of the isotopes of elements not previously found therein or of "unnatural" levels of radioactivity. Atomic warfare might greatly increase the rate of this development. As pointed out earlier in this report, radiostrontium is particularly the element which would cause concern in the latter event. Forage directly contaminated with fallout, if consumed by farm animals soon after deposition, might cause radiation injury from the presence of insoluble radioactive products. Strontium is metabolically similar to calcium and moves into bone and other calcium-accumulating tissues or fluids. Much is known of the relative behaviors of calcium and strontium, but there appears to be no way of wholly preventing strontium retention. There is some evidence that poultry may "decontaminate" or "detoxify" themselves by reason of a continued dilution through transfer to eggshell. In meat animals, certain tissues might be consumable if boned out, but

such an expedient would be beyond the ordinary scope of meat inspection. Dairy products would contain radiostrontium for some considerable time after cows had ingested strontium-containing forage. Moreover, all availabie feeds, in heavily contaminated areas, might contain significant levels of radiostrontium, perhaps for years.

At present it is not possible to say at what level a food, otherwise wholesome, becomes unwholesome or deleterious by reason of the presence of an unnatural burden of radioactivity. There is a great deficiency of requisite data on the long-term biological effects that may follow the ingestion of such foods by animals and man. Situations in which such information might be of great public importance are not inconceivable and possibly inevitable.

The committee therefore urgently recommends that appropriate experimentation be immediately activated to provide specific information about possible total or cumulative biological effects that might follow the ingestion of such foods. It further urges that the planning of such experiments be broadly based and that the development of the experimental designs and details of their subsequent execution be most carefully considered in order that the emerging data will be acceptable as a basis for the crucial decisions th ultimately will have to be taken, and directly of value to the regulatory agencies charged with the protection of the public interest.

Environmental Changes and Ecological Studies

In the decades ahead there is a strong possibility that the general background of radioactivity in agricultural areas will rise. Contributing to this would be fallout, if weapons testing continues, and wastes from nuclear power plants or isotope processing plants. As indicated in the report of another committee, every effort will have to be made to contain radioactive wastes. Atomic warfare or accidents involving nuclear power sources could of course greatly augment the background and pose difficult problems of land use for agricultural purposes. Limited ecological studies are in progress in the vicinity of certain AEC installations, but it may be wise to consider this general problem somewhat more widely and to attempt to establish, through careful sampling, the present background in representative agricultural areas and in their chief crop and livestock products.

Research activities might appropriately be carried out on areas near weapons test sites where substantially greater changes in background would be anticipated. The distribution in the environment, in the soil at various depths, in the vegetation, in the wildlife, in the streams, and so forth would all be pertinent. The rate of accumulation in soil as affected by land use ought to be studied. Forested land, range land, rotation grassland, and plowland, irrigated and nonirrigated, may each present a different situation. It is possible that certain of the state agricultural experiment stations might be in a position to undertake limited surveys of this type on areas likely to be under their control for some considerable time in the future.

The committee recognized clearly that sustained monitoring and ecological research activities of this type are expensive and are not apt to be professionally rewarding to the individuals participating therein because trends and conclusions would emerge only slowly. However, to be able to recognize changes in the levels of radioactivity in the environment and in products removed therefrom, and to follow movements in the system, may well be in the public interest from a long-range viewpoint.

Food Processing

A recent development in food technology, potentially of considerable and possibly of dramatic significance, is the recognition of the fact that radiation can be used as a means of preserving certain foodstuffs or of lengthening shelf life, either unrefrigerated or refrigerated. The radiation source may be gamma rays or high-energy electron beams. No radioactivity is induced in the irradiated material. Feeding experiments to date indicate that foods so irradiated will prove to be suitable and safe for consumption by man. Parasites in meat and meat products can be killed by exposure to penetrating radiation, and undesirable postharvest changes in plant products, such as the sprouting of potatoes, can be delayed.

The prime objective in radiation processing is to destroy microorganisms, or so greatly to reduce the microbial population (radiation pasteurization) that spoilage is long delayed. To accomplish this, very heavy radiation exposures are necessary because microorganisms are much less sensitive to radiation than are animals and higher plants. The food processor is particularly attracted by the fact that the radiation exposure can and should be carried out after packaging.

The acceptability of some radiation-sterilized foods is open to doubt because of the development of off-flavors and changes in odor or in the texture of the tissues. Much of the developmental work in this field, however, has been of a rather empirical nature, and it is possible that through research means may be found to repress some of these undesirable changes.

Although the feasibility of radiation sterilization has been amply demonstrated, the economics of the various processes have not yet been established. This development has largely been financed by the military with the Army Quartermaster Corps as the primary agency involved, but there has been a broad basis of cooperation in industry and elsewhere, with some technical guidance and evaluation by advisory committees of the National Academy of Sciences. Having in mind the magnitude and coherence of the current broad programs in this area, the committee was of the opinion that the potentialities of this use of radiation are being thoroughly explored and that the interests of the food consumer will be adequately protected. At a later date, the committee expects to review particularly the evidence of wholesomeness and acceptability of irradiated foods.

It is commonly said that P. G. Tait laid down the length of a drive on mathematical principles which could not be exceeded, and that his son drove the ball farther. But at that time Tait had not realized the full effect of spin on the ball.—OLIVER LODGE, *in Past Years, an Autobiography. (Young Tait was a golf champion.)*

Walter S. Adams, Observer of Sun and Stars

Born in Syria in 1876 of American parents, Walter Sydney Adams came to the United States at an early age. As a student he acquired a thorough knowledge of astronomy from several of the ablest scientists in the world: Frost at Dartmouth College; Moulton, Laves, and Bolza at the University of Chicago; and Schwarzschild and Seeliger at Munich, Germany. He spent the years 1901–04 at Yerkes Observatory, largely in the spectroscopic measurement of stellar motions. In 1904 when the Carnegie Institution of Washington established the Mount Wilson Observatory, George E. Hale brought Adams to Pasadena, California, as a charter member of the staff. For a few years, he worked with Hale on solar observations, but, after the 60-inch telescope was completed in 1909, virtually all his research was in stellar spectroscopy. After Hale's retirement in 1923, Adams became director of the Mount Wilson Observatory and served in that capacity until 1946. He received many honors for outstanding contributions to astronomy. He died at his home in Pasadena on 11 May 1956.

The sun, unlike the earth, does not rotate as a solid body. It has what might be called a current around the equator in the direction of rotation. Thus, on the equator the period of rotation is less than 25 days, while near the pole it is almost 34 days. Even at the equator, the speed of rotation is only 2 kilometers per second. Hence, in spectroscopic observations, the Doppler displacements to be measured are minute. Adams' numerous measurements at various solar latitudes, made from 1906 to 1908 with the powerful solar instruments on Mount Wilson, set a new standard of accuracy and remain of great value.

Adams took part with Hale in a detailed comparison of spectra of sunspots with spectra of the normal solar disk. The results of measurements of 11,000 spectrum lines made it possible to conclude that sunspots are characterized not only by temperatures lower than those of the surrounding solar surfaces but also by the presence of fairly strong magnetic fields.

In stellar spectroscopy, Adams' main contributions resulted from studies of stellar motions, of stellar spectral classifications and stellar absolute magnitudes and distances, and of gases in interstellar space.

If the spectrum of a star is photographed alongside a known comparison spectrum, the star's speed in the line of sight may be determined by measuring the displacements of the star lines from the positions of the lines in the laboratory spectrum. This method is widely used because it is the only way to measure velocities of distant stars with reasonable accuracy. In the programs carried out by Adams and his coworkers at Yerkes and Mount Wilson, the number of stars whose radial velocities have been measured is about 8000, or approximately half the total number measured by all observers.

In 1914, Adams, in collaboration with a visiting astronomer, Arnold Kohlschütter, found that the absolute magnitude (intrinsic brightness) of many stars can be determined from the relative intensities of certain lines in their photographed spectra. Absolute magnitudes are obviously of fundamental importance in physical studies of stars. Moreover, comparison of the absolute magnitude of a star with its apparent magnitude as seen from the earth yields stellar distances far beyond the reach of direct triangulation from opposite sides of the earth's orbit. The spectroscopic method, applied at Mount Wilson and elsewhere to many thousands of stars, has had extraordinary effectiveness in extending our knowledge of giant and dwarf stars and of galactic structure.

Adams' last extensive program was the detailed study with high dispersion of lines in stellar spectra introduced not by the star's own atmosphere but by the tenuous gases in the abysmal chasms of space traversed by the star's light on its way to the earth. His observations brought out important facts concerning the nature and motions of these interstellar gases. Virtually all the hundreds of spectrograms required for this program were taken and measured by Adams himself.

From these large programs Adams occasionally turned aside, but never for long, to make valuable studies of individual stars such as α Orionis, o Ceti, the companion to Sirius, novae, and many others.

As an observer, Adams was skillful and indefatigable. If he thought a program valuable, he was not deterred by the fact that it was long and arduous. Even when he was director, he spent nearly as much time at the telescope as did any other member of the staff. And he probably spent more time at the microscope, measuring his spectrograms, than he did at the telescope taking them. His industry and concentration on the task in hand resulted in the accumulation of masses of valuable data and in substantial progress toward a more complete comprehension of the starry universe. He had the use of powerful instruments and, as it were, multiplied the advantages by a sustained personal endeavor.

His emotions were not on the surface, but dealings with his associates were characterized by many acts of consideration and kindness. A quiet sense of humor is revealed in his delightful reminiscences, "Early days at Mount Wilson" [*Publ. Ast. Soc. Pacif.* **59**, 213, 285 (1947)].

PAUL W. MERRILL
Mount Wilson and Palomar Observatories, Pasadena, California

John Dalton was not a fluent speaker, and when, as president of the Manchester Literary and Philosophical Society, he had to make a few remarks when the reader of a paper stopped, he is reported to have sometimes contented himself by saying, "This paper will no doubt be found interesting by those who take an interest in it."—J. J. THOMSON, *Recollections and Reflections.*

News of Science

Cigarettes and Cancer

A new study by scientists at the National Cancer Institute shows that the entire cigarette-smoking population of the United States appears to be subject to the same high risk of lung cancer which was found in earlier studies of selected groups of smokers and nonsmokers. This conclusion is reached by William Haenszel, head of the biometry section, and Michael B. Shimkin, chief of the biometry and epidemiology branch, National Cancer Institute. Their report, *Smoking Patterns and Epidemiology of Lung Cancer in the United States: Are They Compatible?* appeared in the June issue of the *Journal of the National Cancer Institute.*

This study represents the first attempt to test the consistency of data derived from a number of studies relating to the risk of smokers developing lung cancer, smoking habits of Americans, and the general distribution of lung cancer in the population. In general, consistency was noted.

The male-to-female ratio of lung cancer deaths, now 5 to 1, represents the highest sex ratio known for any major disease. The adjustment for smoking history brought the sex ratio for lung cancer into line with those observed for other causes of death. The authors further indicated that if smoking is, in fact, a cause of lung cancer, the following two trends should prevail: the rate of deaths from lung cancer for females will rise by 1965, in accordance with the trend to smoking at earlier ages among women; and the increasing rate of deaths from lung cancer for males will slow down by 1965.

Adjustment for different smoking patterns in rural and urban populations accounted for only a part of the urban-rural differences in lung cancer mortality. In the opinion of the authors, this urban-rural discrepancy represents a real finding and is a manifestation of multiple environmental factors in lung cancer.

Data from the Census Bureau survey, taken in February 1955, show a definite trend toward cigarette smoking at earlier ages among males. About 61 percent of men aged 25–34 had smoked cigarettes regularly by age 21, while only 41 percent of the 55–64 age group had taken up regular smoking at that age.

The survey data also show that only a few women were smoking cigarettes regularly before 1930. In the 25–34 age group, 29 percent were regular smokers by 21, while only 2 percent of the 55–64 age group reported to have smoked regularly at that age. All sources of data used in the study agree that lung cancer incidence and deaths are higher in urban than in rural areas, particularly for males.

British and American Engineering Research

Government support of engineering research in American universities is about 100 times that given by Great Britain to British universities. When Donald F. Galloway, research director of the Production Engineering Research Association of Great Britain, delivered the Calvin W. Rice lecture at the recent semiannual meeting of the American Society of Mechanical Engineers, he said: "The total expenditure by the British government and industry on engineering research in the universities probably does not exceed $700,000 per annum, compared with over $70 million by the United States government." He added that the estimated total expenditure for research and development in the United States last year was about $5 billion, compared with about $700 million in Great Britain, and that research work employs about 500,000 persons in the United States and about 60,000 in Great Britain.

NSF Expands Soviet Translation Program

The National Science Foundation has announced expansion of its program for the translation into English of Soviet research literature. A grant of $76,500 for this purpose has been awarded to the American Institute of Physics. The expanded program will include the *Zhurnal Tekhnicheskoi Fiziki* (*Journal of Technical Physics*), *Akusticheskii Zhurnal* (*Acoustics Journal*), and physics articles from the *Doklady Akademii Nauk SSSR* (*Proceedings of the USSR Academy of Sciences*). First issues of the translated journals will appear this summer.

Subscription prices for the new journals are as follows: *Journal of Technical Physics,* approximately 4000 pages per year, $90; *Acoustics Journal,* approximately 500 pages per year, $20; *Proceedings of the USSR Academy of Sciences* (physics articles only), approximately 900 pages per year, $25.

The foundation and the American Institute of Physics have already successfully collaborated in the publication of *Soviet Physics—JETP,* a bimonthly translation of *Zhurnal Eksperimentalnoi i Teoreticheskoi Fiziki* (*Journal of Experimental and Theoretical Physics*), six issues of which have now appeared.

In addition to the program in physics, NSF is supporting translations of Soviet papers in mathematics and biology; and plans for 1957 include the earth sciences and the engineering sciences. The American Mathematical Society publishes about 1000 pages annually of Soviet work under the title, *American Mathematical Society Translations.*

The foundation has just awarded a small grant to *Biological Abstracts* for the translation and publication of abstracts from the Soviet journal, *Referativnyi Zhurnal: Biologiia* will be translated by Consultants Bureau, Inc., of New York and reprinted in *Biological Abstracts.* The abstracts will be drawn from 31 primary journals covering a wide range in the field of biology.

Free Neutrino Found

Evidence for the existence of the free neutrino has been collected by Frederick Reines and Clyde Cowan, Jr., of the Los Alamos Scientific Laboratory, which is operated for the U.S. Atomic Energy Commission by the University of California. The existence of the free neutrino, a particle without charge and with vanishingly small mass, was postulated more than 20 years ago by Nobel laureates Enrico Fermi and Wolfgang Pauli in order to account for the disappearance of energy from the radioactive process known as beta decay.

In a statement of congratulations for the discovery, Willard F. Libby, commissioner and acting chairman of the AEC, said: "Detection of the neutrino by scientists at Los Alamos Scientific Laboratory and the Savannah River Plant of the U.S. Atomic Energy Commission is of great importance to nuclear research. The Commission congratulates the scientific team . . . on its magnificent accomplishment. . . .

"One of the greatest mysteries facing scientists today is the nature of the 'glue'

which holds atomic nuclei together. Discovery of the neutrino should help scientists to gain understanding of this force, which is one of the fundamental properties of matter."

The first scientific publication about the discovery will be a paper by Reines and Cowan which will appear in an early issue of *Science*.

Survey of Engineering Professors

The engineering colleges of the United States have experienced a net loss of 3 percent of their professors to industry within a 2-year period, and this at a time when the engineering colleges need 1300 more teachers to carry the 1956–57 load. This situation was reported to the American Society for Engineering Education by an industry committee headed by A. R. Hellwarth, assistant to the director of employment, Detroit Edison Company.

The committee, acting under the ASEE Relations with Industry Division, reported a net 2-year loss of three professors in each hundred from campuses to industrial employers, with higher salaries being the major lure. During the 2-year period more than 750 left engineering faculties for industry, but 500 left industry for teaching positions.

The survey was based on figures submitted by 62 percent of the 150 colleges and universities accredited by the Engineers' Council for Professional Development. These institutions recorded a gain in teaching strength from 8000 to 8400 during the period, in spite of losses to industrial employers. The present shortage of 1300 would require the engagement of 15 additional professors or instructors for every 100 now teaching.

Mammary Tumor Agent in Mice

In a 10-year study of the occurrence of mammary tumors in more than 4000 female mice of various specific genotypes, scientists at the National Cancer Institute have been able to change the susceptibility of certain strains to breast tumors by genetically controlling the transmission of the mammary tumor agent. This agent, or virus, is also known as the "milk factor," because some 20 years ago a series of experiments at the Jackson Memorial Laboratory, Bar Harbor, Me., disclosed a maternal influence in mouse breast cancer.

When the young of a high-cancer strain mouse were foster-nursed by a female of a low-cancer strain, the young failed to develop cancer at the appropriate age as would have been expected. The experiment was then reversed, and many mice later developed breast cancer. These studies indicated that some factor in the milk was inciting the cancer, and that this "factor" or "agent" seemed to have many characteristics of a virus.

In the search for the specific gene or genes responsible for the transmission of this "milk factor," three strains of mice were used: one that possessed the tumor agent and was genetically susceptible to it; one that did not have the agent but was genetically susceptible to it; and one that neither had the agent nor was susceptible to it. By a system of matings involving cross-breeding, genetic material of the resistant strain was introduced into a susceptible strain and progressively increased in succeeding generations.

The authors, Walter E. Heston, Margaret K. Deringer, and Thelma B. Dunn of the Laboratory of Biology, National Cancer Institute, believe that evidence is at hand indicating that the agent does not remain inactive over a number of generations only to suddenly reappear; the agent did not appear intrinsically or *de novo*; and not all mammary tumors of the mouse are associated with the agent and not all mice with the agent develop tumors. The presence of the agent merely increases the probability that a tumor will occur and its absence decreases this possibility.

News Briefs

■ Heart disease, which causes more deaths in the United States than any other disease, does not rank among the top three most serious illnesses in any Asian country. In Asia, the top killers are epidemic diseases and others such as tuberculosis, beri-beri, cancer, malaria, yaws, and pneumonia.

In Japan, heart disease was the fifth most frequent cause of death in 1954 with a rate of 59.8 per 100,000, the highest rate in Asia. In the United States in 1950, 745,074 persons died of heart disease—a rate of 494.4 per 100,000 population. In 1953, this jumped to 794,120 deaths—a rate of 501.4 per 100,000.

■ The United Nations Educational, Scientific and Cultural Organization has announced that an experimental solar still to remove minerals from water has been erected at Mildura in Australia. The device consists of a glass structure set over a shallow trough of black plastic. Water to be treated is siphoned into the trough and evaporated by the sun shining through the glass canopy. The vapor condenses and drains into storage tanks. It may be possible to use the still to provide an inexpensive method of purifying water from artificial wells for agricultural and household uses in areas that receive little rainfall.

■ The first house in Britain to be heated by solar energy will be ready for occupancy in September. The special heating equipment, details of which are secret, is being installed. Leslie Gardner of the Western Detail Manufacturing Company Ltd., Bristol, is the inventor of the system and designer of the house. He will be visiting the United States this summer, probably in mid-August, when he will go to Detroit and Chicago in the hope of interesting American industrialists in his idea.

■ The nation's new $750,000 magnetic observatory and laboratory opened recently at Fredericksburg, Va. It replaces the old magnetic observatory at Cheltenhem, Md.

■ Both the United States and the Soviet Union have officially endorsed Vienna as the site of headquarters for the proposed International Atomic Energy Agency.

■ Pakistan has started the construction of a national science institute at Lahore, the United Nations Educational, Scientific and Cultural Organization reports. Recently representatives from Australia, India, Britain, the Soviet Union, and the United States attended a ceremony for the laying of the cornerstone.

The institute, the Ismail Science House, is to be completed in a year. It will have a library of 250,000 works, Pakistan's first comprehensive scientific library. It also will have a bibliographic and documentation center, a modern auditorium, a research center, a press and publication department, offices for scientific societies, club rooms, and a cafeteria.

■ The Woods Hole Oceanographic Institution has spent $200,000 converting the former Coast Guard cutter *Crawford* for hurricane research. The vessel left on 1 July for a 6-week cruise.

The *Crawford*, which is 125 feet long and 23 feet wide, has been air-conditioned and is capable of carrying food for 1 month for a crew of 14 and an 8-man scientific staff. The ship has two laboratory areas, and her scientific equipment includes a deep-sea winch with 25,000 feet of 5/32-inch wire, radar, two Long Range Navigation sets (Loran), a Raytheon shallow water echo-sounder, an Edo deep water echo-sounder, a special precision echo-sounder recorder developed at Woods Hole, two small winches for temperature measurements down to a depth of about 1000 feet, a continuously operated motion picture camera that will photograph the sea surface by exposing one frame every second, sea temperature measurement devices,

an instrument to measure the height of the cloud ceiling at night, and a small house for radiosonde balloons to record wind speed at high altitudes.

Scientists in the News

IRENE M. STRIEBY, library consultant at Eli Lilly and Company, has received the 1956 Professional Award of the Special Libraries Association. She was honored for "her outstanding professional achievements and in recognition of her devotion to the cause of special libraries for a quarter of a century."

Mrs. Strieby joined Lilly in 1934 to become head of its library. Under her leadership the library has been expanded to include a research library, a business service, and several departmental collections; the number of volumes has grown to 30,000; and the staff of librarians has been increased to 18.

ARTHUR M. BUECHE has been named manager of a newly created unit in the chemistry research department of the General Electric Research Laboratory, Schenectady, N.Y. The unit, which will be devoted to polymer and interface studies, will be part of the Physical Chemistry Section. Bueche has been a member of the research laboratory staff since 1950.

Cecilia Payne-Gaposchkin has been appointed professor of astronomy at Harvard University. She is the first woman to attain full professorship at Harvard through regular faculty promotion. Since 1938 she has been Phillips Astronomer in the Harvard College Observatory and lecturer on astronomy.

Dr. Payne-Gaposchkin and her husband, Sergei I. Gaposchkin, are a team in astronomical research. Together they have made an extensive survey of variable stars.

CONRAD G. MUELLER, JR, associate professor of psychology at Columbia University, has been awarded a senior postdoctoral fellowship in physiological psychology for the academic year 1956–57. This fellowship, which is administered by the National Academy of Sciences–National Research Council, is supported by the Carnegie Corporation of New York.

Mueller's main interest is in the psychophysiology of vision. On July 1, he started work at the Rockefeller Institute for Medical Research, where he is conducting research on physiological mechanisms in vision, acquiring additional techniques for the micropipette method of recording from single sensory cells, and employing other techniques for working with the vertebrate retina.

RAYMOND OLNEY, who has served since 1921 as editor and publisher of *Agricultural Engineering*, the journal of the American Society of Agricultural Engineers, has received the 1956 Max Eyth medal, which is awarded by the Max Eyth Society for the Advancement of Agricultural Engineering (a German Society). The medal was presented in Roanoke, Va., during the 49th annual dinner of ASAE.

Other awards presented at the dinner are as follows: the John Deere gold medal, ARTHUR W. CLYDE, College Park, Pa., and two Cyrus Hall McCormick gold medals, one to MARTIN RONNING, Minneapolis, Minn., and one to H. P. SMITH, College Station, Tex.

JAY W. FORRESTER, head of the digital computer division of Lincoln Laboratory at Massachusetts Institute of Technology, has been appointed professor of industrial management in the M.I.T. School of Industrial Management. While at Lincoln Laboratory, and earlier in the Servomechanisms Laboratory at M.I.T., Forester developed the method of random access magnetic storage that is now the standard memory device for reliable, high-speed digital computers.

Another appointment at M.I.T. is that of I. EDWARD GARRICK of the National Advisory Committee for Aeronautics who will serve for a year as the Jerome Clarke Hunsaker professor. He will teach and conduct research in the department of aeronautical engineering, concentrating on studies of flutter, aerolastic problems, and aerodynamic phenomena.

ROBERT W. BEAL has been named director of development at the Corps of Engineers Research and Development Laboratories, Fort Belvoir, Va. In the newly created position, Beal, formerly chief of the mechanical engineering department, will be responsible for the establishment of an applications engineering program designed to bridge the gap between research and development and the quantity production of new military equipment for the Corps of Engineers.

CARL B. KOFORD, zoologist at the Museum of Vertebrate Zoology, University of California, has been appointed resident naturalist of the Smithsonian Institution's Canal Zone Biological Area, a tropical forest and wildlife preserve on Barro Colorado Island. He succeeds JAMES ZETEK, who recently retired after 45 years of service in the Canal Zone. During most of this time Zetek was associated with the U.S. Department of Agriculture and the Smithsonian Institution.

ERNEST YEAGER, associate professor of chemistry and technical director of the Ultrasonics Research Laboratory at Western Reserve University, and IRA J. HIRSH, research associate for the Central Institute for the Deaf and associate professor of psychology at Washington University (St. Louis), received the biennial award of the Acoustical Society of America during the recent meeting in Boston of the International Congress on Acoustics. The award, consisting of a medal and a check, this year was given jointly for the first time since it was first conferred in 1942.

WILLIAM E. ADAMS, the James Nelson and Anna Louise Raymond professor of surgery at the University of Chicago, has accepted an invitation to be a visiting lecturer at the University of Glasgow in Scotland. His appointment, which is under the Fulbright program, began on 1 July.

JOHN A. D. COOPER, associate professor of biochemistry at Northwestern University Medical School, will direct a course this summer at the University of Brazil, Rio de Janeiro, on radioisotope techniques in biology and medicine. He also will make a 3-month lecture tour of South American universities and scientific societies. His trip is being sponsored by the U.S. Department of State.

MAX C. BREWER of the geophysics branch of the U.S. Geological Survey at Menlo Park, Calif., has been appointed director of the Arctic Research Laboratory at Point Barrow, Alaska. The University of Alaska operates the laboratory under contract with the Office of Naval Research. The new director will assume his duties in September, approximately 1 month before IRA L. WIGGINS, present director, returns to Stanford University, where he is professor of biology and director of the Natural History Museum.

ROBERT F. MEHL, director of the Metals Research Laboratory and head of metallurgical engineering at Carnegie Institute of Technology, has been awarded the "Grand" medal of Le Chatalier by the council of the French Society of Metallurgy. The medal will be presented in Paris during the society's annual symposium on metallurgy, 22–27 Oct.

JOHN R. REES, for 12 years a mechanical engineer for the Navy Bureau of Aeronautics, has joined the staff of the Engineering Metrology Section of the National Bureau of Standards. He will aid in the preparation of handbooks and various other publications on screw threads and screw-thread gaging.

DALE R. CORSON has been appointed chairman of the department of physics at Cornell University. Corson joined the Cornell faculty in 1946. He is a consultant to the General Electric Advanced Electronics Center and to several panels and study groups in the Department of Defense. For two periods recently he has been on the research staff at California Institute of Technology.

JULIUS A. STRATTON, now vice president and provost of Massachusetts Institute of Technology, has been appointed to the newly established post of chancellor of the institute. As chancellor, he will administer the academic program in all its parts, and all academic officers will come under his jurisdiction. In addition, he will act as deputy to the president, who is the institute's chief executive officer. Stratton will serve as the general executive officer for all institute affairs, and in the absence of the president, he will perform all the duties and functions of that position.

JULIAN S. SCHWINGER, professor of physics at Harvard University, will be a visiting professor of physics and mathematics at Stanford University this summer. He will lecture on "Differential equations of field theory."

The following are among those who have recently received honorary doctoral degrees.

Princeton University: HENRY EYRING, dean of the graduate school and professor of chemistry at the University of Utah; RAJKUMARI A. KAUR, Minister of Health for India.

Rutgers University: WILLIAM SHOCKLEY, director, Shockley Semiconductor Laboratory of Beckman Instruments, Inc.

Wayne University: GEORGE RIEVESCHL, JR., scientific assistant to the president of Parke, Davis and Company; LAWRENCE REYNOLDS, chief of staff and chairman of the executive committee of Harper Hospital, Detroit.

Denison University: GEORGE M. LYON, manager of the Veterans Administration hospital at Huntington, W.Va.

MAURICE EWING, professor of geology and director of Lamont Geological Observatory, Columbia University, has been elected to foreign membership by the Royal Netherlands Academy (Section for Sciences).

The New York Academy of Medicine has announced the appointment of GERTRUDE L. ANNAN as librarian, succeeding JANET DOE who is retiring. Miss Annan has been associate librarian for the past 3 years and previous to that was curator of the Malloch Rare Book and History Room of the academy library.

Miss Doe is retiring from her position as librarian after 30 years of service to the New York Academy of Medicine and to the library profession. Her outstanding leadership has won her recognition in many forms. She has served as president of the Medical Library Association and as a member of the committee that surveyed the Armed Forces Medical Library. She was presented with the Marcia C. Noyes award for outstanding achievement in medical librarianship. Among her many professional contributions are her bibliography of Ambroise Paré and her editorship of two editions of the *Handbook of Medical Library Practice*.

Recent Deaths

NICHOLAS C. ARTSAY, Valhalla, N.Y.; 68; mechanical engineer; 20 June.

WILLIAM S. BRYANT, New York, N.Y.; 95; retired authority on otology and otolaryngology; 26 June.

ALBERT W. CLAFIN, Providence, R.I.; 71; president of Rhode Island College of Pharmacy and Allied Sciences; 18 June.

PASQUALE V. DI COSMO, Wildwood Shores, N.J.; 51; president and chief engineer of Cosmo Engineering Laboratories, Inc.; 25 June.

PAUL H. DIKE, Huntington Valley, Pa.; 78; retired assistant director of research for Leeds and Northrup; 25 June.

CHANNING R. DOOLEY, Summit, N.J.; 78; expert on industrial training; president of the *Training Within Industry Foundation*; 25 June.

CECIL E. EDDY, Melbourne, Australia; 56; director of the X-ray and Radium Laboratory of Melbourne; chairman of the United Nations Scientific Committee on the effects of atomic radiation; 27 June.

P. MAURICE GLASOE, Northfield, Minn.; 82; professor emeritus of chemistry at St. Olaf College; 15 June.

FRANK E. MALLON, Brooklyn, N.Y.; 61; clinical associate professor at the College of Medicine of the State University of New York; 24 June.

JAMES M. NAUL, Plainfield, N.J.; 68; electrical engineer; 23 June.

VLADIMIR A. OBRUCHEV, Moscow, U.S.S.R.; 93; leading Soviet geologist and geographer; president emeritus of the Geographical Society of the U.S.S.R.; research authority on the permafrost phenomenon; 19 June.

WILLIAM B. PLANK, Morgantown, Pa.; 70; mining engineer and founder of the mining engineering department of Lafayette College; 19 June.

HOWARD E. PULLING, Kennebunk, Me.; 70; plant physiologist; professor of botany at Wellesley College; 24 April.

RUDOLF RUEDEMANN, Albany, N.Y.; 91; former paleontologist of the State Museum (New York); 18 June.

FRANKLIN A. STEVENS, New York, N.Y.; 65; associate in medicine at the Columbia University College of Physicians and Surgeons; 19 June.

Education

■ St. John's University, Brooklyn, N.Y., has broken ground for a Science-Pharmacy Hall on its Long Island Division Campus at Hillcrest, Jamaica. Approximately $4 million has been allocated for the construction and partial equipment of the new unit, which will accommodate 1200 students at one time with 600 classroom seats and 600 laboratory stations. The building is expected to be ready for occupancy for the start of the fall term in 1958.

■ Lowell Technological Institute will participate in the observance of the Perkin Centennial by holding a celebration, 26–28 Sept. During that period a lecture and display of rare books will be featured, and at a special convocation honorary degrees will be conferred. There will be a dedication ceremony for one of the institute's newest buildings, and the program will culminate in a day-long open house.

■ The U.S. Atomic Energy Commission has announced that it will make available plutonium-beryllium neutron sources for subcritical assemblies used by nonprofit educational institutions engaged in training and research in the nuclear sciences. Loan of plutonium-beryllium neutron sources is an extension of a current AEC policy to make available certain materials for subcritical assemblies without a use-charge to the institution involved.

■ The use of entomology as a teaching medium in high-school biology courses was studied recently at Michigan State University. A survey questionnaire sent to 200 Michigan high schools brought replies from 135 teachers. Of the 135 schools represented by the replies, 97 percent include an average of 2½ weeks of insect study in biology courses, 93 percent study "the place insects have in our lives," 90 percent study "basic insect structure," 81 percent study various individual insects, 65 percent use some of the order names, and 15 percent study methods of insect control.

Although 81 percent of the schools have collecting equipment and 68 percent have laboratory equipment such as cages and aquaria, only 51 percent take field trips regularly, only 41 percent

make collections each year, and only 23 percent have any type of science club. The survey indicated that overcrowded facilities and overcrowded schedules cause some neglect of time-consuming activities such as field trips, class projects, and science clubs. It also indicated that some teachers have not received adequate training in making collecting equipment, handling aquaria, conducting field trips in urban areas, rearing insects, and selecting keys suitable for high-school use. It is expected that this information will prove useful in revising entomology courses offered to prospective teachers.—SHIRLEY TOUSCH, *Department of Entomology, Michigan State University, East Lansing.*

■ The Atomic Energy Commission, and the National Science Foundation, have jointly announced the establishment of a second Summer Institute on Nuclear Engineering for engineering college faculty members. The institute is at the Brookhaven National Laboratory and is under the joint sponsorship of NSF, the AEC, and the American Society for Engineering Education. Thirty students from 22 institutions are enrolled in the 2-month course, which was established to accommodate applicants who could not be admitted to the first institute because of space limitations. The first institute is being conducted by the Argonne National Laboratory School of Nuclear Science and Engineering; 60 faculty members from 36 colleges and universities are participants.

The National Science Foundation has made funds available to pay stipends to those attending these institutes and to defray travel expenses. The funds for those attending the Argonne National Laboratory institute will be administered by Northwestern University, and the funds for those attending the BNL institute will be administered by Associated Universities, Inc. No tuition will be charged.

■ Last month Sen. Herbert H. Lehman urged the U.S. Department of Agriculture to consider a site near Cornell University for a new animal disease laboratory. The suggestion was made in a letter from Lehman to the Secretary of Agriculture.

■ Progress is being made in the organization of the U.S. Army Mathematics Research Center that is being established at the University of Wisconsin. R. E. Langer of the university's mathematics department has been appointed director of the center; a contract for its operation was recently negotiated between the university and the Army; and an Army steering group has been named that is headed by Col. Paul N. Gillon, commanding officer of the Office of Ordnance Research.

The center is expected to operate at an annual cost of approximately $800,000. At present its offices are located within the university's mathematics department; however, ultimately it will occupy a major part of a new building.

The permanent staff of the center will be kept small. It will be supplemented by a gradually rotating corps of scientists from Army facilities and from academic institutions who will visit the center for varying periods of time.

■ Bryn Mawr College has received a gift of $25,000 from the Radio Corporation of America in recognition of its work "in providing advanced training for women in the physical sciences." This is the largest single donation Bryn Mawr has ever received from industry. The gift will be added to a fund for the construction of the new Science Center, which will be devoted to advanced training in chemistry, physics, and mathematics, as well as in biology and geology.

■ The Western Technical Writing Institute, specifically organized to teach engineers how to write, is being established at 465 E. Union St. in Pasadena, Calif. In addition to offering courses in technical writing and editing, the institute will conduct research in technical communication techniques. Faith Kildare, teacher and author of *Fundamentals of Professional Writing,* will direct the institute with the aid of an advisory board of industrial editors and technical writing directors.

In the Laboratories

■ A temporary laboratory has been leased in San Diego by the Convair Division of the General Dynamics Corporation to implement the company's new basic research program. Six of the 25 to 30 scientists who ultimately will comprise the staff, already are on the job.

The temporary laboratory is being equipped for explorations in gas dynamics, aerodynamics, theoretical and experimental physics, physical chemistry, mathematics, and metallurgy. It will consist of a main laboratory of 1200 square feet; a 200-square-foot chemical laboratory, an instrument shop, and six offices, including those of the director of scientific research, Charles L. Critchfield, and his assistant, W. H. Dorrance. The laboratory will be permanently housed in Convair's new $40-million Atlas intercontinental ballistic missile facility near Montgomery Field by the last quarter of 1957.

■ A revised stable isotopes inventory and price list is available from Oak Ridge National Laboratory, which the Union Carbide and Carbon Corporation operates for the U.S. Atomic Energy Commission at Oak Ridge, Tenn. Changes in this catalog were made in accordance with the new distribution policy set forth by the AEC earlier this year.

Under the old distribution policy, electromagnetically enriched isotopes were only lent to users in the United States. Although this loan procedure limited their uses, it provided isotopes at very reasonable cost to the user. Also, many of the isotopes were returned to stock after expiration of the loan period and could be made available to new users. Because it would be impractical to lend isotopes to certain foreign users, a limited sales policy has been in effect for the past 2 years.

The revised procedures provide for the outright sale of many enriched stable isotopes to all domestic users, as well as to certain foreign users, and permits the loan of samples of rare and expensive items under certain conditions. Moreover, neither domestic nor foreign applicants will be required to file and obtain AEC approval before purchasing the materials.

■ San Diego, Calif., has given a tract of land on the city's northern limits to the General Atomic Division of General Dynamics Corporation for the construction of a nuclear research laboratory. In accepting the gift, John J. Hopkins, president of General Dynamics, expressed gratitude to the citizens of San Diego for their "approval of our proposal to found here a Laboratory for Pure and Applied Science, and for the most generous offer of the land on which to build it. It is our hope that the new General Atomic Laboratory will not be concerned with last year's atomic products or with yesterday's atomic technology. Rather we are dedicated to the development of completely new products, to the pursuit of completely new thoughts, to the establishment of completely new technologies. . . ."

■ The new research reactor at Armour Research Foundation of Illinois Institute of Technology has gone into operation. This is the nation's first private nuclear reactor for industrial research. It will enable industry to conduct reactor studies without security restrictions and military competition.

Built by Atomics International, a division of North American Aviation, Inc., the machine is housed in a new $1.25-million Physics and Electrical Engineering Research Building. It is not intended for the generation of electrical power, nor for research on reactors themselves. Probably its most frequent use will be in the production of radioactive samples.

The reactor is a "water boiler" type

capable of operating at a power level of 50 kilowatts. It uses fuel in the form of a water solution of uranyl sulfate—approximately one kilogram of U-235. The fuel has been obtained from the Atomic Energy Commission on "extended loan," as required by law.

Twenty-four companies are participating in the nuclear reactor research program at Armour Research Foundation. Under the participation plan, each firm is contributing $20,000 toward the construction and initial operation of the $700,000 reactor facility. A.R.F. is providing the remaining funds. The companies will share in the benefits of a 3-year program whose aim is the application of atomic techniques to industrial problems.

■ The Atomic Energy Commission has announced plans for a gas-cooled power reactor experiment at the National Reactor Testing Station in Idaho. Proposals to participate in the reactor experiment project will be invited at an early date from qualified firms. The initial phase of the project calls for design of the reactor experiment.

The experiment, which is expected to cost an estimated $4 million over a period of several years, is intended to develop engineering data and experience for design and construction of military package power reactors and small civilian central station power plants.

The gas-cooled reactor is the eighth type chosen by the commission for research and development work in the program to achieve economic reactor power systems for civilian application as well as for possible military applications. The reactor experiment project will be administered by the AEC's Chicago Operations Office.

■ A Du Pont Company survey shows that one of every seven of its employees is a college graduate. The number nearly doubled in 8 years—to 14,000—while the total of employees went up about 15 percent to approximately 100,000, including those at government-owned plants operated by the company. In 1947 about one employee in 10 had a college degree. In the same period the company's total of wages and salaries went up 85 percent—to $491 million last year.

■ The Raytheon Manufacturing Company has purchased a 15-acre site in Goleta, Calif., 5 miles west of Santa Barbara, for a new engineering laboratory to be used in the design and development of airborne electronics and infrared equipment. Raytheon already has a few employees working in temporary space in Santa Barbara. The company plans to transfer 40 to 50 additional employees during July from its Chicago equipment laboratory, which will be discontinued after the transfer is completed. Eventually the engineering group is expected to total approximately 125.

Miscellaneous

■ Private firms interested in the peaceful development of atomic energy face an "almost incomprehensible maze" of state laws and regulations that may impede their activity. This is one of the major conclusions of *State Regulations of Atomic Energy,* first published section of an analysis of atomic energy and the law that is being carried out by the University of Michigan Law School.

The volume, which is financed by the Michigan Memorial-Phoenix Project, is designed to give private enterprise a check list of the legal problems that may be encountered in atomic energy development. It also suggests how states can "bring order out of chaos" in this new field. Written by E. Blythe Stason, Samuel D. Estep, and William J. Pierce of the Michigan Law School, the book terms "confusing and overlapping jurisdictions" of state agencies interested in the health and safety aspects of atomic energy as "undoubtedly the most significant aspect of the state regulatory pattern" which may affect atomic industrial development.

■ Technion, the Israel Institute of Technology, in Haifa, has announced openings for professors in the following fields: structural engineering, hydraulic engineering, soil engineering, mechanical engineering (with special qualifications in machine design and applied thermodynamics), industrial management and production engineering, electronics, chemical engineering, aeronautical engineering, mathematics, physical chemistry, general and inorganic chemistry, and basic and industrial design. Applications with full details should be sent in duplicate to Efraim Margolin, technical director, American Society for Technion, 1000 Fifth Ave., New York 28, N.Y.

■ Copies of the report by the Engineers Joint Council entitled *Professional Standards and Employment Conditions* are available without charge from Engineers Joint Council, 29 W. 39 St., New York 18, N.Y. In a statement accompanying the report, Thomas H. Chilton, president of the council, says:

"The report represents the labors of many thoughtful people who have considered and discussed the problems of engineers as employees. . . . It is, therefore, not the work or view of any one individual. . . . Important responsibilities of the professional engineer, employers of engineers, engineering societies, and engineering educators are identified in the report. Each of us as professional engineers, and all others directly or indirectly associated with the profession, must strive diligently to establish a clear understanding of employment conditions necessary to meet professional employee expectations. An employment environment which encourages full professional and technical development of employed engineers is essential to the advancement of the profession, and the realization of their fullest contribution to the economy."

■ In commemoration of the 50th anniversary of the passage of the 1906 Pure Food and Drugs Act, the library of the New York Academy of Medicine has prepared an exhibit of books, pamphlets, and periodicals on the adulteration of food and drugs in the United States and on legislative measures to protect the consumer. A section is devoted to Harvey W. Wiley, founder of the 1906 Act. The exhibit will be shown at the academy from 12 June until 1 Oct.

■ The National Multiple Sclerosis Society has announced that for the first time abstracts of the world's current literature on demyelinating diseases will be available in English to scientists here and abroad. This service is made possible by an initial grant of $15,000 by the National Society to the Excerpta Medica Foundation, Amsterdam, Holland. The foundation will excerpt from all current scientific and medical journals, foreign as well as American.

The results will be published in a monthly journal containing 100–150 abstracts. M. W. Woerdeman will supervise the project, while G. W. F. Edgar will direct the staff in Amsterdam. A 10-man editorial board of scientists has been appointed to oversee the work.

■ "Gyotaku—the Impression of a Fish," an exhibition that represents a blending of science and art, is being shown at the American Museum of Natural History in New York until 4 Sept. A Gyotaku is an impression taken of an actual fish. The result is a form of decoration that can also serve as a labor-saving scientific tool. According to Francesca LaMonte, associate curator of fishes at the American Museum, the Gyotaku is more useful to ichthyologists than a photograph in investigating certain details such as scale count, which must usually be done from the actual specimen.

The prints that are on display are a selective sampling of the work of the members of Gyotaku-no-Kai (Friends of Fish Print), an organization of artists and ichthyologists that is under the leadership of Yoshio Hiyama, an ichthyologist at the University of Tokyo.

Reports

Relation of Ammonia Excretion to Urine pH in the Guinea Pig

In 1856 Claude Bernard (*1*) observed that the urinary *p*H of carnivorous animals is markedly lower that that of herbivorous animals. Some years later Walter (*2*) described the excretion of ammonia in various animals that had been rendered acidotic and stressed the protective and base-saving features of this mechanism. Since then, numerous studies on the patterns of ammonia excretion in man, dog, and rat, especially during acidosis, have been published. On the other hand, very few studies on these patterns in the rabbit have been made and, as far as we are aware, none in the guinea pig. The current theories of ammonia excretion are, therefore, largely based on studies in species that normally excrete an acid urine.

In spite of much work in this field, three major questions await conclusive answers. What is the physiological stimulus for ammonia excretion? What is the relative importance of enzymatic and physicochemical factors in the mechanism of ammonia excretion? What is its physiological significance? During studies on ammonia excretion in the guinea pig, we have made observations that are surprising when they are considered in the light of present concepts of ammonia formation and excretion.

The ammonia output of guinea pigs (1 to 4 microequivalent/30 min kg) is low compared with that of rats or dogs and varies with age, sex, and dietary habits. In acute experiments (*3*) guinea pigs were rendered acidotic or alkalotic; and urine, collected under oil, was analyzed for *p*H (*4*) and ammonia content (*5, 6*). The urinary ammonia concentration was expressed as microequivalents per milliliter and the output as microequivalents per 30 minutes, per kilogram of body weight. Data from seven acute experiments are plotted on Fig. 1, using the urinary *p*H as abscissa and ammonia concentration or output as ordinate (*7*). The graph shows that both the concentration and the relative output of ammonia in the urine rise, not only during acidosis as in man, dog, and rat, but also during alkalosis. The same is true if the relative ammonia output for each animal per 30 minutes is plotted against the *p*H. The correlation between deviations of *p*H from the normal range and increased ammonia output is not strict but is statistically significant. A similar pattern has been observed in a few experiments with rabbits.

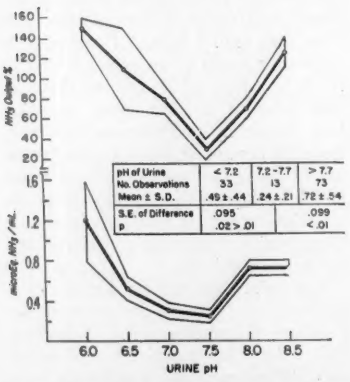

Fig. 1. The relation of ammonia excretion to urine *p*H in the guinea pig.

The increased ammonia concentration in alkaline urines cannot be explained as a function of urine flow, as could an increased output. It must, therefore, be assumed that there is increased ammonia production or transfer into alkaline, as well as acid, urine.

These observations suggest reconsideration of current hypotheses regarding the stimulus. Decreased plasma bicarbonate or *p*H or increased titratable acidity or decreased *p*H of the urine have been proposed as the proximate stimulus for the increase in ammonia output during acidosis. None of these, however, could cause the marked increase in ammonia output observed during alkalosis. Information now available does not indicate whether the same or different stimuli act during acidosis and alkalosis.

Ammonia excretion is currently considered to be the resultant of two independent mechanisms, one being enzymatic, the other being physicochemical in nature. Investigations during the past few years indicate that glutaminase activity in the kidneys is one of these factors (*8*). Transport of ammonia from tubular cells into urine, be it by passive diffusion (*9*) or active exchange for sodium (*10*), is held to be the second limiting factor for ammonia excretion. Our experiments demonstrate that ammonia excretion in the guinea pig is nearly as efficient in the alkaline as in the acid range. It seems improbable, therefore, that physicochemical transport is the limiting factor in ammonia excretion in the guinea pig. If it were, different mechanisms in the acid and alkaline ranges would have to be postulated.

At urine *p*H's of 8, 8.5, and 9 the fractions of ammonia present in an un-ionized form as free ammonia are respectively 4, 11, and 29 percent (*11*). Back diffusion of the ammonia during the flow of the urine from the distal tubules to the bladder should, therefore, also be taken into account in studies on ammonia excretion in the alkaline range. This aspect has not yet been explored.

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3. The animals were anesthetized with pentobarbital and ether, and a stomach tube and bladder catheter were inserted. They were given $NaHCO_3$ or HCl by stomach tube. The experiments lasted 2 to 6 hours, and 6 to 15 urine samples were collected during each experiment.
4. Determinations of *p*H were done with a Cambridge Research *p*H meter using the syringe-type glass electrode.
5. A modification of the microdiffusion method of D. Seligson and H. Seligson [*J. Lab. Clin. Med.* 38, 324 (1951)] was used. The working range of this method in our hands was between 0.5 and 100 microequivalents of ammonia nitrogen.
6. This investigation was supported by a research grant, RG-3795, from the National Institutes of Health, U.S. Public Health Service.
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25 January 1956

Taming and Susceptibility to Audiogenic Convulsions

Several recent papers have reported that taming influences both growth and behavior in the albino rat. Tamed animals are described as larger, heavier, and more resistant to the effects of physical and emotional stress than untamed ones. They have also been characterized as

Table 1. Frequency of *N*, *R*, *C* responses, mean frequency and intensity scores, median latencies of first running, and epileptoid attacks in tamed and nontamed rats.

Group	No.	*N*	*R*	*C*	*F*	*I*	Latencies trial 1st running attack	Latencies trial epileptoid phase
Nonhandled	16	48	59	53	0.70	0.65	26.5	84.5
Handled	8	36	41	3	0.55	0.55	40	Indeterminate
Handled prior to test	7	39	22	9	0.44	0.48	62	Indeterminate

more active and less fearful, and they are poorer hoarders but better learners (*1–6*).

The purpose of the present experiment was to reevaluate the relationship between taming and audiogeic seizures. Previously reported differences are possibly confounded by differences in strain, and endocrine or nutritional status or both (*7*). In addition, currently available data are in conflict. One study (*8*) associates taming with low susceptibility, while a second claims tamed animals to be more sensitive to convulsion (*9*).

The experimental subjects were 31 albino rats of a strain inbred by the department of physiology, Emory University Schools of Medicine and Dentistry, for about 25 years, 47 days of age at the time of the first test. Sixteen, the untamed group, were whelped in a lightproof, extremely quiet room and separated into individual cages at weaning. They were touched only when they were transferred once a week to clean cages and when they were placed in and removed from the test chamber. This involved briskly picking up each animal by the tail. They were exposed to light and noise only during the test period. In contrast, the 15 tamed animals (originally there were 16 but one died) were reared in the regular colony room. At weaning, they were segregated three to a cage and subjected to taming. This consisted of 5 minutes of handling each day, the animal being petted, fondled, and allowed to crawl about in the experimenter's lap. Taming was continued throughout the experiment. In addition, seven were given 2 more minutes of petting just prior to being tested to determine whether a drastic change in treatment enhanced sensitivity. All were allowed free access to Purina Lab Chow and water from the time of weaning.

The animals were tested by being placed in a metal container inside a sound-resistant box and exposed to 2 minutes of noise (average level, 101 db; range, 90 to 104 db) generated by a 4-inch doorbell. Each animal received ten tests on alternate days. During each test the latencies of the first running attack and of the epileptoid seizure were recorded when these responses occurred. After each test the subject's test behavior was rated on a three-point scale from *N* (nonreaction) through *R* (running attack) to *C* (epileptoid convulsion). Frequency (*F*) and intensity (*I*) scores were derived from the data of the ten tests according to the following equations:

$$F = \frac{R + C}{N}; I = \frac{R(0.50) + C(1.00)}{R + C}.$$

The rationale of these scores and the criteria defining response categories is presented in an earlier paper (*10*). Table 1 presents a summary of these data.

Since the frequencies of *N*, *R*, and *C* ratings were derived from ten tests on 31 animals, the statistical criterion of independence is violated, making a chi-square evaluation impossible. The mean *F* and *I* scores were compared by means of Student's *t* test for small independent samples. Because there were animals in both tamed and untamed groups that did not react on any test, certain of the latencies were indeterminate. Median latencies are therefore reported, and statistical evaluation was accomplished by the Mann-Whitney *U* test for independent groups of unequal *N*.

Inspection of Table 1 suggests that taming has a protective effect directly proportional to its magnitude or immediacy or both. This conclusion, however, is not borne out by the statistical evaluation of the data. There is no reliable difference between the tamed group and the tamed group that was given further handling just before tests (*F* scores: $t = 0.65$, $P > 0.50$; *I* scores: $t = 0.44$, $P > 0.60$). When the scores of these two groups are pooled and compared with those for the unhandled group, differences in all but one case again lack significance. (*F* scores, $t = 1.58$, $P > 0.10$; *I* scores, $t = 1.39$, $P > 0.10$; latency per trial per running attack, $U = 161$, $P < 0.10$; latency per trial per epileptoid phase, $U = 168.5$, $P < 0.04$). Thus taming can be said to have a protective effect only in the sense that the tamed animals require a longer time to have a full-blown epileptic fit.

The basis of these negative results is a matter for speculation. They are probably not due to insufficient handling, since the amount given the present animals compares favorably with that reported in previous studies (*2*, *8*). One possibility lies in the strain used. Our rats, derived from Wistar stock, are extremely docile, gentle, and easily handled. It is possible that the petting given the tamed groups could add only an insignificant increment to already maximally tame subjects. Inspection of the wide variability in responsiveness in both handled and nonhandled groups meanwhile suggests that much larger samples would be required to demonstrate the suggested beneficial effects of handling on seizures. Should this be the case, its importance to an understanding of the seizure mechanism is probably limited.

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13 February 1956

Protoplasmic Streaming in Plants Sensitive and Insensitive to Chilling Temperatures

Many plant species of tropical and subtropical origin are subject to chilling injury when exposed to temperatures below about 10°C but above their freezing points. Severity of injury generally increases as chilling temperature decreases and as duration of exposure increases. Symptoms may develop during or after exposure.

In a study of physiological responses associated with chilling (*1*), I made some observations on protoplasmic streaming. Effects of temperature on streaming were observed by Sachs (*2*), who noted that streaming ceased at about 11°C in *Cucurbita pepo* and *Lycopersicon esculentum*, both of which are chilling-sensitive plants. In contrast, Sachs cited observations by previous workers that in several lower plants streaming ceased at or near 0°C. This suggests differential responses by chilling-sensitive and chilling-insensitive plants.

In the present work, the influence of chilling temperatures on streaming was observed in cells of young petiole trichomes of several species. Observation of individual cells was possible by moving the microscope, mount, and light, as a unit from one constant-temperature room to another. A fan blew air across the stage to insure rapid temperature equilibrium and to reduce heating of the subject from the illumination. In all the chilling-sensitive plants observed—tomato (*Lycopersicon esculentum*), watermelon (*Citrullus vulgaris*), honeydew melon (*Cucumis melo*), a tobacco (*Nicotiana glutinosa*), and sweetpotato (*Ipomoea batatas*)—streaming ceased or was just perceptible after 1 or 2 minutes at 10°C. Invariably it ceased promptly at 5° or 0°C. In contrast, streaming in the chilling-insensitive plants observed—radish (*Raphanus sativus*), carrot (*Daucus carota*), and filaree (*Erodium cicutarium*)—proceeded at 0° or 2.5°C.

For tomato trichomes, increasing the exposure at 0°C delayed increasingly the resumption of streaming on transfer to 20°C. If exposure to 0°C exceeded about 24 hours, streaming failed to resume in most trichomes. In contrast, streaming in filaree proceeded slowly but steadily at 0°C for up to 3 days. On transfer back to 20°C, rapid streaming was resumed in 1 or 2 minutes.

In addition to these effects on streaming, chilling caused other responses. After 2 days of chilling at 0°C, some trichome cells of tomato were plasmolyzed. In others, the protoplasts formed into aggregated clumps, and small particles executed Brownian movement in the cell sap. Such movement was never observed in unchilled trichomes. This structural disorganization of the protoplast by chilling may result from syneresis of the protoplasmic gel, as has been suggested for a slime mold (*3*).

The striking difference described here between chilling-sensitive and chilling-insensitive plants suggests an association between susceptibility to chilling injury and cessation of streaming. Chilling injury and cessation of streaming may be separate symptoms of some more fundamental disorder that is induced at 10°C or below in chilling-sensitive plants. Alternatively, the visible symptoms of chilling injury could be effects secondary to cessation of streaming.

The contrasting effect of chilling temperatures on streaming in cells of sensitive and insensitive plants may reside in a differential effect of temperature on one or more of the following: cell lipids (*4*) and their role in structure and action of the protoplasm; energy supply from respiration to maintain protoplasmic streaming; energy utilization for streaming; or protoplasmic viscosity. If the mechanism of streaming is related to an adequate supply of adenosine triphosphate (*5*), some interesting comparative biochemistry for chilling-insensitive and chilling-sensitive plants is suggested.

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6 March 1956

Direct-Reacting Bilirubin, Bilirubin Glucuronide, in Serum, Bile, and Urine

Since the introduction into clinical chemistry of diazotized sulfanilic acid for the determination of serum bilirubin, it has been recognized that bilirubin occurs in two different forms, one giving a so-called "direct" reaction, the other exhibiting a so-called "indirect" reaction in which coupling takes place only after the addition of alcohol (*1*). In general, when the jaundice is due to excessive destruction of hemoglobin, as it is in hemolytic anemia, most of the bilirubin in serum is of the indirect-reacting form. If the jaundice results from intrahepatic or extrahepatic obstruction to the passage of bile into the intestine, most of the bilirubin in serum is of the direct-reacting form.

Various explanations have been offered to account for this clinically important difference, but the experimental evidence in support of these theories has been controversial (*2*). Recent studies have shown that direct-reacting bilirubin obtained from serum or bile is water-soluble over a wide *p*H range, whereas the indirect-reacting pigment is practically insoluble in water below a pH of 8 (*3*). It has been suggested that the solubility in water of the direct-reacting fraction may be the result of a conjugation of bilirubin with a polar substance (*1, 4*). Because of their instability, satisfactory chromatographic purification of these pigments, particularly the direct-reacting fraction, has not been achieved (*4*).

This difficulty has now been overcome by studying (*5*) the more stable dipyrromethene diazonium pigments, which were obtained by treating serum and urine from jaundiced patients or normal bile with an excess of diazotized sulfanilic acid that was dissolved in dilute hydrochloric acid. In this reaction 1 mole of bilirubin reacts with 2 moles of the reagent, yielding 2 moles of hydroxypyrromethene diazonium salt (*6*).

After preliminary purification and butanol extraction, the azo-pigments obtained from serum, bile, and urine were separated and purified by ascending paper chromatography, employing a solvent system that consisted of 75 parts ethyl methyl ketone, 25 parts *n*-propionic acid, and 30 parts water. By using this system, it was found that direct-reacting bilirubin in the serum of jaundiced patients and almost all of the bilirubin in fresh bile and in the urine of jaundiced patients gave rise to an azo-pigment (B) exhibiting an R_f value of 0.25 to 0.30. On the other hand, the azo-pigment (A) obtained from indirect-reacting serum bilirubin, crystalline bilirubin, and heated bile exhibited an R_f value of 0.45 to 0.50. Diazonium salts of synthetic neoxanthobilirubinic acid and isoneoxanthobilirubinic acid (*7*) were found to have an R_f value that is identical with that of indirect-reacting serum bilirubin and that of crystalline bilirubin. Absorption spectra in the visible range appeared to be identical for azo-pigments A and B.

Hydrolysis of repeatedly chromatographed azo-pigment B in 1*N* hydro-

Table 1. Acid and enzymatic hydrolysis of conjugated hydroxypyrromethene diazonium salt (azo-pigment B). (Values are given in micromoles.)

Substrate azo-pigment	Type of hydrolysis	Product	
		Azo-pigment	Glucuronic acid
B, 0.41	1*N* HCl, 1 hr at 100°C	A, 0.41	0.39
B, 0.10	β-glucuronidase*	A, 0.083	0.09
B, 0.70	β-glucuronidase†	A, 0.61	0.58
B, 0.23	β-glucuronidase† (heat-inactivated)	B	< 0.01
B, 0.36	Concentrated sulfuric acid	Destroyed	0.38
A, 0.55	1*N* HCl, 1 hr at 100°C	A	< 0.01

* Beef liver β-glucuronidase (Warner-Chilcott), 24 hr at 37°C and *p*H 4.6.
† Bacterial β-glucuronidase (Sigma, Lot No. 125–63), 24 hr at 37°C and *p*H 6.2.

chloric acid for 1 hour at 100°C resulted in its complete conversion to azo-pigment A. For each micromole of hydrolyzed azo-pigment B, 1 μmole of glucuronic acid was liberated, as determined by the carbazole method (*8*). Data of a typical experiment are given in Table 1. Hydrolysis could also be achieved by incubating azo-pigment B with β-glucuronidase of animal or bacterial origin (Table 1).

Since fresh bile and urine from jaundiced patients yielded almost exclusively azo-pigment B, and since 2 moles of hydroxypyrromethene diazonium salt are produced from 1 mole of bilirubin (*6*), it would appear that direct-reacting bilirubin is conjugated with 2 moles of glucuronic acid. In analogy with other instances of glucuronide formation, it may be assumed that the glycosidic linkage occurs at the α,α'-hydroxy groups of bilirubin. The finding in bile and urine of minute amounts of material giving rise to azo-pigment A together with azo-pigment B suggests that small amounts of direct-reacting bilirubin may be present as a monoglucuronide. This observation is in agreement with an earlier report, indicating the separation of two closely related water-soluble fractions of bilirubin from bile (*9*). While this work was in progress, Billing and Lathe published an abstract in which they also suggest that, in bile, bilirubin is excreted as an "ester glucuronide" (*10*).

In the serum of patients with regurgitation jaundice, conjugated bilirubin was found to predominate (direct-reacting bilirubin). On the other hand, in retention jaundice, most of the serum pigment was shown to be free bilirubin (indirect-reacting bilirubin). Since, in jaundiced patients with bilirubinuria, the urinary bilirubin was found to yield almost exclusively azo-pigment B, it appears that the kidneys can excrete only conjugated bilirubin. In a child with congenital nonhemolytic jaundice, exhibiting 30 mg percent of free bilirubin in the serum (*11*), no bilirubin could be found in the urine (*12*).

These findings demonstrate that, in the serum, glucuronic acid-conjugated bilirubin gives the direct van den Bergh reaction, whereas free bilirubin, owing to its insolubility in water, requires the prior addition of alcohol to initiate the coupling with the diazo reagent. In bile, most or all of the bilirubin is excreted as a water-soluble glucuronide. In regurgitation jaundice, conjugated bilirubin gains access to the blood and hence to the urine, resulting in bilirubinuria.

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30 April 1956

Solute and Temperature Effects in the Pervaporation of Aqueous Alcoholic Solutions

The phenomenon of pervaporation was first observed by Kober (*1*), who originated the term. It may be defined as the passage of a liquid through a semipermeable membrane and subsequent evaporation of the liquid. Farber (*2*) pointed out the usefulness of pervaporation in concentrating protein solutions. More recently, pervaporation and related phenomena have been discussed by da Fonseca (*3*).

Although the few available references cite the advantages of using pervaporation in certain chemical and biological researches, this technique has not been used to any great extent. In connection with food studies, we have used pervaporation to dehydrate mashed potatoes. Our methods may also be applicable in phases of other research—for example, in dehydrating plant tissue or in removing water from aqueous alcoholic extracts.

When a solution of equal parts by weight of ethanol and water was placed in a cellophane bag that was suspended in a forced-draft oven maintained at 60°C, the water content of the aqueous alcohol that passed through the membrane was about 65 percent. (The bags were formed from seamless, regenerated cellulose that is manufactured specifically for dialysis. Although wall thickness was not critical, a 0.0016-in. membrane was ordinarily used.) However, when a suspension of mashed potatoes in 1/1 ethanol-water was treated in the same manner, the water content of the pervaporated vapor was about 95 percent. Essentially the same result was obtained when the filtrate from a mixture of mashed potato, ethanol, and water was pervaporated, indicating that the higher ratio of water to alcohol must be due to the presence of the soluble potato solids.

Soluble potato solids consist principally of sugars, citric and other organic acids, nitrogen compounds, and inorganic salts. The naturally occurring mixture of water-soluble potato solids is also soluble in 1/1 ethanol-water but is only slightly soluble in ethanol.

To study the effect of the presence of a solute on the pervaporation of an aqueous ethanol solution, 1/1 ethanol-water mixtures containing various solutes (2.5 percent added) were pervaporated. Some of these solutes (class I) are soluble in ethanol and represent various degrees of solubility in water. Other solutes (class II) are soluble in water and are only slightly soluble in ethanol. The solubilities of the various solutes in water and in alcohol and the percentages of water in the transmitted vapor are listed in Table 1.

Our class-I solutes included citric acid, hydroquinone, and benzoic acid; although citric acid is quite soluble in water, hydroquinone is moderately soluble, and benzoic acid is only slightly soluble. In pervaporating solutions containing class-I solutes, the percentage of water in the pervaporated vapor varied somewhat, increasing (but not proportionally) as the solubility of the solute in water increased. With citric acid added to the aqueous alcohol mixture, the water content (66 percent) of the pervaporated vapor was the same as that of the mixture without added solute. However, in the presence of the solutes

Table 1. Relationship of solute solubilities (*6*) to percentage of water in pervaporated vapor.

Solute	Solubility (g/100 g solvent)		Water in transmitted vapor (%)
	In water	In ethanol	
Control			66
Class I			
Benzoic acid	0.29 (20°C)	52.5 (20°C)	59
Hydroquinone	7.2 (20°C)	49.8 (20°C)	64
Citric acid	163.4 (25°C)	62.1 (25°C)	66
Class II			
Dextrose	97.6 (23°C)	0.22 (23°C)	81
Sodium chloride	36.0 (20°C)	0.07 (18.5°C)	82
Sodium citrate	92.7 (25°C)	0 (25°C)	96

Table 2. Effect of temperature and solute on the pervaporation rates of water and ethanol.

Pervaporating liquid	Temperature (°C)	Pervaporation rate (g/in.² hr)			Water (% in pervaporated vapor)
		Water	Ethanol	Total	
Water	25	0.42		0.42	
	45	1.31		1.31	
Ethanol	25		0.08	0.08	
	45		0.49	0.49	
1/1 Water-ethanol	25	0.32	0.34	0.66	48.5
	45	0.88	0.45	1.33	66.2
1/1 Water-ethanol (with 2 percent sodium citrate)	25	0.25	0.01	0.26	96.1
	45	0.81	0.02	0.83	97.6
1/1 Water-ethanol (with 2 percent benzoic acid)	25	0.15	0.24	0.39	38.5
	45	0.74	0.53	1.27	58.3

that are only moderately or slightly soluble in water, the water content of the pervaporated vapor was less than that of the control, being 64 and 59 percent for hydroquinone and benzoic acid, respectively.

Class-II solutes included dextrose, sodium chloride, and sodium citrate. The percentage of water in the transmitted vapor was much greater in every case with these latter solutes present than that in the control, being 81 to 82 percent for dextrose and sodium chloride and 96 percent for sodium citrate. In the presence of the class-II solutes, the percentage of water in the transmitted vapor apparently increases with progressive insolubility of the solute in ethanol.

A chamber was built to obtain more precise data related to the solute and temperature effects on the pervaporation rates of water and alcohol. It consisted of an aluminum cylinder 1 in. long with an inside diameter of 3.5 in., which was closed with membranes at the ends. Two aluminum rings with gaskets attached were used to clamp the cellophane membranes in liquid-tight seals. Two holes were provided in the wall of the cylinder, one for a reservoir tube and the other for a thermometer.

Experiments were carried out using water, ethanol, 1/1 ethanol-water, a 1/1 ethanol-water solution that contained 2 percent sodium citrate, and a 1/1 ethanol-water solution that contained 2 percent benzoic acid. Two temperatures, 25°C and 45°C, were utilized in a forced-draft oven. The pervaporation chamber was weighed, sampled initially, and sampled again after 3 hours. The percentage of water in the samples was determined by a modification of the Karl Fischer method (*4*). The pervaporating solution was stirred continuously by means of a magnetic stirrer. The data obtained are presented in Table 2.

When ethanol and water are pervaporated separately, the ethanol-pervaporation rate increases more rapidly with a rise in temperature than does the water rate. However, when a 1/1 mixture of the two are pervaporated, different results are obtained. At the lower temperature, the presence of water enhances the passage of the ethanol, increasing its pervaporation rate from 0.08 to 0.34 g/in.² hr (Table 2). At the higher temperature, the rate of ethanol is approximately the same (0.49 to 0.45 g/in.² hr), regardless of whether water is present. The net effect of the temperature increase from 25° to 45°C, when a 1/1 aqueous ethanol solution is pervaporated, is to increase the percentage of water in the pervaporated vapor from 48.5 to 66.2.

The presence of 2 percent sodium citrate (water-soluble, ethanol-insoluble) in a 1/1 solution of ethanol and water decreases the ethanol pervaporation rate to a barely detectable level but decreases the water rate only slightly. The net effect is to increase the water content of the pervaporated vapor from 48.5 percent (control) to 96.1 percent, when one is operating at the lower temperature, and from 66.2 percent (control) to 97.6 percent at the higher temperature (Table 2).

The net effect of benzoic acid (water-insoluble, ethanol-soluble) is opposite to, but less pronounced than, that of sodium citrate. The water rate is reduced considerably, while the ethanol rate is reduced only slightly at the lower temperature and is even increased at the higher temperature. The net effect is a decrease in the percentage of water in the pervaporated vapor from 48.5 to 38.5 percent at 25°C and from 66.2 to 58.3 percent at 45°C (Table 2).

From thermodynamics, one would expect that the presence of a water-soluble, ethanol-insoluble solute would enhance the evaporation of ethanol from a water-ethanol mixture. An experiment involving evaporation from an open dish (no membrane) was conducted at 25°C, in which mixtures of equal parts of ethanol and water, with and without 2 percent sodium citrate, were evaporated for 6 hours in a forced draft (*5*).

As expected, the addition of sodium citrate resulted in a slight reduction of the water-evaporation rate (from 0.07 to 0.05 g/in.² hr) and a slight increase in the ethanol rate (from 1.05 to 1.10). Thus, interposition of a membrane at 25°C with sodium citrate present reversed the composition of the vapor from 96 percent ethanol to 96 percent water (Table 2). The total pervaporative rate of aqueous alcohol without solute present at 25°C (Table 2) was about half the total evaporative rate of the same mixture without a membrane.

The "solute effect" must be due to interfacial phenomena. The following explanation is postulated. As the solution is pervaporated, solute molecules either adhere to, or become trapped in, the membrane. Probably the latter is the case, since the solution is stirred vigorously during the pervaporation. The "good" solvent, by means of interaction with the solute molecules, can readily pass through the membrane. The "poor" solvent is repelled from the solute molecules, and its passage through the membrane is thus restricted.

If this hypothesis is correct, then a membrane impregnated with solute should give a "solute effect" until the solute is gradually dissolved from the membrane if it is used in the pervaporation of a water-ethanol mixture. Conversely, if the solute is in the mixture and a clean membrane is used, the "solute effect" should increase with time. This was shown to be the case in two experiments. First, a membrane soaked overnight with a saturated aqueous solution of sodium citrate was used to pervaporate a 1/1 solution of aqueous ethanol. After 2 hours the water content of the pervaporated vapor was 82 percent, and at 4 hours it had dropped to 64 percent. Then a 1/1 aqueous ethanol solution containing 2 percent sodium citrate was pervaporated at 45°C for 8 hours, with hourly sampling. The ethanol rate, which was very low at the beginning, was reduced to zero by the third hour.

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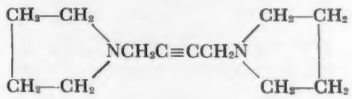
15 March 1956

Tremor Induced by Tremorine and Its Antagonism by Anti-Parkinson Drugs

During the course of screening drugs in mice, it was observed that 1,4-dipyrrolidino-2-butyne (Tremorine)



produces a profound tremor of the head and limbs lasting for more than 1 hour. In addition, the animals move about slowly, show rigidity, and are less active. Parasympathetic stimulation is marked and characterized by profuse salivation, miosis, diarrhea, and bradycardia. A profound fall of body temperature also occurs. Sustained tremor is a rare phenomenon of drug action (in our experience, less than 10 of 10,000 drugs tested).

Because of the possible usefulness of such a drug in testing for anti-Parkinson agents, further studies have been carried out. In mice, doses of 20 mg/kg given orally, intraperitoneally, intravenously, or subcutaneously are effective, the tremors appearing within 10 to 30 minutes, depending on the route, and lasting 3 to 4 hours. Such drugs as atropine, scopolamine and other anti-Parkinson agents control the tremor and cholinergic effects completely in one dose of 2 to 10 mg/kg. They are effective either given prior to Tremorine or after full tremor effects are evident. Methantheline will control the parasympathomimetic effects but does not affect the tremor; thus the central and peripheral actions of the drug can be separated. Central depressants such as the barbiturates, mephenesin, alcohols, anticonvulsants, and analgesics are ineffective against the tremor in doses less than those causing marked ataxia, sedation, or hypnosis. Hexamethonium and TEA were also ineffective. These results emphasize the specificity of the antagonism of Tremorine tremor by the anti-Parkinson drugs in contrast to nicotine tremor which is ephemeral, has both central and peripheral components, and may be controlled by a wide variety of agents (*1*).

Tremorine in dogs has effects similar to those observed in mice. In the dog, a dose of 5 mg given intraperitoneally gives a full picture of Tremorine action. In the monkey, tremor is not as marked as it is in dogs, but it is easily seen and the Parkinsonlike facial changes are very striking. Tremorine action in the dog and monkey develops within the first hour. The tremors last for 24 hours or more and parasympathetic stimulation lasts for 2 or 3 days. Repeated doses of atropine or other anticholinergic agents will control these effects. Tremorine is often fatal in dogs and monkeys because of respiratory complications if adequate treatment is not given.

Twenty analogs of Tremorine were tested. None produced tremor. This suggests a high degree of chemical specificity for the production of these effects.

The site of action of Tremorine is under investigation. The tremor occurs in decerebrate rats, mice, and rabbits. Tremor also appeared in a chronic completely decerebellate dog, superimposed on the much coarser and slower tremor normally present in this animal (*2, 3*).

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7 March 1956

Another Case of Anomalous Pregnancy in a White Rat

Evans (*1*) reported a few specific instances of anomalous pregnancies in rodents and suggested that the phenomenon might be more common than a review of relevant literature would indicate. In four unequivocal cases (one in a rat, two in mice, and one in a guinea pig), the animals, although they were segregated from the time that pregnancy was observed until the time that the young were of weaning age, delivered a second litter.

In our laboratory, female rats are invariably isolated in heavily meshed individual cages as soon as pregnancy is observed. A case of anomalous pregnancy was noted in 1955, but detailed records are not available. However, another unequivocal case of anomalous pregnancy was observed and recorded in 1956. A healthy seven-pup litter was delivered by albino rat XX (Wistar strain) on 21 Jan. 1956, each member of which has survived to date. On 11 Feb. 1956, this rat produced a healthy eight-pup litter, each member of which was still alive at 16 days of age. The first litter consisted of three males and four females, and the second consisted of three males and five females.

Thus, 23 days elapsed between the production of the first and second litters. For at least 6 days before the birth of the first litter, rat XX was securely isolated, and from parturition until the birth of the second litter, it was segregated from all except its own immature offspring. With these, it shared a cage until 2 days before the birth of the second litter.

Evans discusses critically two theories explanatory of such anomalous pregnancies, namely, delayed implantation at the blastocyst stage, which is said to occur sporadically in rodents, and superfetation. Evans thought that the superfetation hypothesis was unlikely in the case of her rat, since the interval between its litters (25 days) was greater than the average gestation period. If the essential criterion for superfetation is a shorter-than-normal gestation period, the superfetation hypothesis does not seem relevant to the case of our rat, where the 23-day interval between the delivery of litters represents, according to Farris (*2*), a gestation period that is well within the normal range.

If the delayed implantation hypothesis were invoked in the case of rat XX, it would have to be assumed that the blastocysts had survived during the first pregnancy, been retained in the uterus during labor, and implanted after delivery of the first litter. Boyd and Hamilton (*3*) discuss lengthened gestation in lactating rodents in relation to physiological delay of implantation, but, in the case of our rat, the period seems improbably prolonged.

Another possibility is tentatively suggested. Rat XX was segregated 6 to 7 days before the birth of the first litter, and the total time between segregation and the birth of the second litter was thus 29 to 30 days. Farris (*2*) says that gestation may be extended a week or more if a female is carrying a large number of young and is suckling a litter. Thus, if it were possible for a pregnant female to be inseminated, this may have occurred just before segregation, and the 29 to 30-day gestation period does not constitute an improbable gestation period for a multiparous rat that is suckling a seven-pup litter. Although the sizes of the litters renders this explanation unlikely, the remote possibility that this rat may have been fertilized by way of the other uterine horn is nevertheless suggested for consideration.

It is finally suggested that the literature on parthenogenetic development in unfertilized rat eggs, as, for example, Austin and Braden (*4*), might be considered in relation to recorded cases of anomalous pregnancies.

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29 February 1956

Pathology of Egg-Adapted Avian Encephalomyelitis

The viral etiology of a disease of chicks that is characterized by a fine tremor of the upper body, bilateral ataxia, or both was first reported by Jones (*1*) in 1932. Knowledge of avian encephalomyelitis (AE), or epidemic tremor, as summarized by Olitsky and Van Roekel (*2*), has remained limited, principally because of the difficulty of propagating the virus by intracerebral inoculation of chicks.

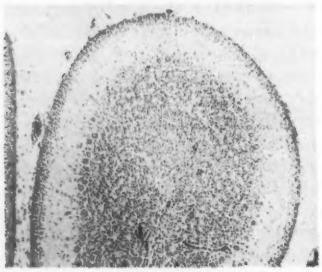

Fig. 1. Cerebellar folium of normal 20-day-old embryo (×38.7).

Fig. 2. Cerebellar folium of 20-day-old embryo inoculated with AE virus (×38.7). Severe edema of central white matter.

For control, wing-web vaccination of growing birds with a live chick-propagated virus has been suggested (*3*) for conferring passive immunity upon the offspring. From the academic point of view, AE virus is of interest by virtue of its relation to the polio group of viruses, in the tentative classification of Burnet (*4*), on the basis of its neurotropic character and ether resistance (*5*).

In previous studies in this laboratory (*6*) with a highly chick-adapted strain (*7*), AE virus was shown to be transmissible to adult birds by both the intraperitoneal and the intraocular route and to maintain itself in the allantoic cavity of developing chicken embryos for 6 to 7 days. Many attempts, however, to demonstrate multiplication of the virus by the egg technique have failed. In analogy with the experience in adult birds, AE virus, in the form of 0.05 ml of a 10-percent-chick-brain suspension in buffered saline at *p*H 7.2, was injected into the eye of 11-day-old embryos. Egg-adaptation was thereby achieved (*5*), as was demonstrated by serial passages in eggs, reproduction of the disease in chicks with egg-propagated virus, neutralization of the virus in eggs and chicks by AE immune serum, and specific pathologic alterations in the embryos.

Intraocular injection of embryos was made by cutting a circular window over the border of the air cell, applying a drop of sterile mineral oil to the shell membrane, and exerting a sharp jab in the direction of the eye with a 1.5-in., 20-gage needle attached to a 0.25-ml tuberculin syringe. After the window was sealed with Scotch tape, the eggs were incubated at 37°C for an additional 9 days. During this period, the eggs received no further turning, except for daily candling. Losses during the first 4 days after inoculation were considered incidental deaths and amounted to about 11 percent of the inoculated eggs.

By the use of a pooled suspension of embryonic eye and brain, the virus has undergone 11 passages by the intraocular route with an average titer of 10^{-5}. Material from the fourth passage was also inoculated into the allantoic cavity of 9-day-old embryos and incubated for an additional 11 days. This series has undergone nine passages with an average titer of 10^{-2}. Beginning about 6 days after inoculation, embryos inoculated by either route exhibited decreased movement and, occasionally, retardation of growth. When they were opened on the 20th day of incubation, most embryos were alive, as was established by a persistent heartbeat, but were either partially or completely immobilized. Control embryos, which were not inoculated or were inoculated by either route with buffered saline, eye-brain suspension, or allantoic fluid from normal embryos, failed to show this syndrome.

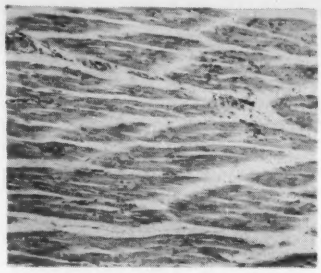

Fig. 3. Skeletal muscle of normal 20-day-old embryo (×79).

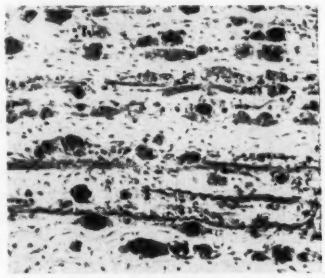

Fig. 4. Skeletal muscle of 20-day-old embryo inoculated with AE virus (×79). Severe muscular dystrophy.

Histopathologic examination of embryos in five to six coronal sections disclosed changes that were uniform in character but variable in intensity and location and consisted of encephalomalacia and muscular dystrophy. Of 48 embryos inoculated with AE virus, 45 exhibited significant alterations in the central nervous system and 43 in the skeletal musculature.

The nervous lesions were characterized by severe focal edema to the point of total destruction of the ground substance, with the margins of the lesions occasionally displaying early gliosis, vascular proliferation, and pyknosis. There was little evidence of ischemic necrosis. The anatomic areas of predilection were, in order of falling frequency, cerebellum (Figs. 1 and 2); striata; diencephalon; mesencephalon; nuclei of cranial nerves III, V, and VIII; and lumbar cord.

The muscular changes were represented by eosinophilic swelling and necrosis, fragmentation, and loss of striation of affected fibers, with rare sarcolemmal proliferation and heterophil infiltration (Figs. 3 and 4). The occipital and upper cervical musculature was chiefly involved, especially in the dorsal aspects.

Of 21 control embryos, seven had mild focal edematous lesions in the distal white matter of the central cerebellar

folia and in four isolated dystrophic fibers in the dorsal group of the occipital musculature.

The findings (*8*) were of interest for the following reasons: intraocular injection of embryos succeeded in egg-adaptation of a virus hitherto not cultivable by the egg-technique; the virus-induced lesions resembled the well-known pathologic expressions of E-hypovitaminoses in domestic birds (*9*); and the nonspecific lesions were similar to, and the specific lesions more extensive than, those observed by Love and Roca-Garcia (*10*) in egg-adapted poliomyelitis.

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13 March 1956

Crystallization of Cytidine Diphosphate Choline from Yeast

Evidence for the role of a new coenzyme, cytidine diphosphate choline (CDP-choline), in one of the biosynthetic pathways of lecithin synthesis was recently presented by Kennedy and Weiss (*1*), who had been working with mammalian liver preparations. This compound has now been isolated from extracts of baker's yeast, and the purified compound has been crystallized as the sodium salt from 80-percent ethanol at *p*H 8.5 (*2*). Purification was by adsorption and elution with acetone from charcoal, followed by chromatography on a column of Dowex-1, formate form (10-percent crosslinked; eluant, 0.01*M* formic acid). CDP-choline was crystallized, in the form of thin, diamond-shaped plates with parallel or nonparallel sides, from the combined fractions obtained between seven and nine resin-bed volumes of eluant. The crystals decomposed, starting at 250°C, without melting. The absorption spectrum (peak at 280 mμ, $\lambda 280/\lambda 260 = 2.08$, $\lambda 290/\lambda 280 = 0.74$, at *p*H 2) was identical with that of cytidine-5′-phosphate (C5P) (*3*) and the E_m 280 mμ at *p*H 2 = 13.0 .

The compound was tentatively identified as the monosodium salt of CDP-choline on the basis of analytic values (*4*) of cytosine, pentose, acid-labile phosphate, total phosphate, choline, and Na^+ of 1.00, 0.99, 0.00, 1.96, 0.92, 1.05, respectively. Choline was estimated spectrophotometrically according to the procedure of Appleton *et al.* (*5*) after acid hydrolysis (40 minutes at 100°C in 1*N* HCl) and treatment of the hydrolyzate with the acid phosphatase of semen (*6*).

The absence of additional carbon- or nitrogen-containing moieties was indicated by elementary analysis (*7*) of the crystals considered to be the monosodium salt of the compound. Calculated percentage composition values were C, 32.88; N, 10.96; P, 12.12; and H, 4.93. Values found were C, 32.45; N, 10.98; P, 12.20; and H, 4.96.

The content of C5P was studied after acid hydrolysis (1*N* HCl, 40 minutes at 100°C). Paper chromatography (solvent, 3 parts 1*M* ammonium acetate at *p*H 7.5 in 0.003*M* Versene and 7.5 parts 95-percent ethanol, *8*) of an aliquot of the hydrolyzed sample (1.75 μmole) revealed the disappearance of the ultraviolet-absorbing starting material (R_f = 0.23) and the appearance of a new ultraviolet-absorbing spot (R_f = 0.12). The new compound was identified as C5P (1.59 μmole) on the basis of its R_f and absorption spectrum and by its conversion with 5′-nucleotidase (*9*) to inorganic phosphate (1.53 μmole) and cytidine (1.47 μmole, R_f = 0.53 with the afore-described solvent system.

After removal of the C5P with Norit from an aliquot of the hydrolyzed sample (1.75 μmole), treatment with semen phosphatase released 1.76 μmole of inorganic phosphate and 1.54 μmole of choline. Choline could not be detected in the hydrolyzed sample before treatment with the phosphatase preparation or in the unhydrolyzed compound following treatment with the enzyme.

The presence of a pyrophosphate linkage was evidenced by cleavage of the compound with nucleotide pyrophosphatase (*10*). Acid phosphatase of semen and 5′-nucleotidase, on the other hand, did not attack the compound.

The crystalline compound was found by Kennedy and Weiss to undergo enzymatic pyrophosphorolysis (*1*) at an identical rate with that of synthetic CDP-choline and could not be distinguished from the synthetic P^{32}-labeled compound by anion-exchange chromatography. The possibility that the CDP-choline is contaminated with a small amount of cytidine diphosphate ethanolamine has not been eliminated.

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28 March 1956

Nucleic Acid and Succinic Dehydrogenase of Rat Liver after X-irradiation

In the course of an investigation of the effect of x-irradiation on animal tissues, the succinic dehydrogenase levels, as well as the nucleic acid composition of livers from control and from irradiated rats, were ascertained and compared (*1*). Earlier work in this laboratory disclosed that, when unfiltered x-radiation of dosages up to 20,000 r is applied to the surviving liver of rats just after partial hepatectomy, the extent of liver regeneration is not altered over an 11-day observation period. Pathologic changes of varying intensity, however, were noted in those livers when they were subjected to an x-ray dosage of 20,000 r (*2*).

Adult male rats of the Sprague-Dawley strain were placed under pentobarbital anesthesia. The abdomen of each rat was incised and the entire liver was exteriorized. The liver was held in position by leaded rubber rings secured at the base, the remainder of the body then being completely shielded with lead. The liver was irradiated with x-ray for 10 minutes (total dosage, 6500 r). The x-ray source comprised a 140-kv therapy machine operating at 8 ma [half-value layer,

3.92 mm Al; distance, 12.5 cm; 650 r/min (air)].

The controls were manipulated in a similar manner, except that no radiation was applied. The animals were maintained in individual cages, and ground Dixie cubes and water were administered *ad libitum*. At periods of 1, 2, 5, and 11 days, the respective groups of control and irradiated rats were sacrificed by decapitation, and the livers were extirpated. Small sections were removed for histological examination, and the remainder was reserved for succinic dehydrogenase or nucleic acid analyses. In one series, a 0.50-percent cysteine diet, prepared by incorporation of the hydrochloride (Merck) into the powdered control ration, was fed to rats 2 weeks prior to surgery and over a 48-hour period preceding necropsy.

For the determination of succinic dehydrogenase, each of the liver samples was homogenized with 0.067*M* phosphate buffer at pH 7.4 (*3*). The enzyme content was ascertained manometrically in a Warburg assembly at 37.5°C (*4*), according to the procedure of Schneider and Potter (*5*). The method used for the determination of nucleic acids was based on the phosphorus content (*6*). The respective dry-liver powders, prepared by the scheme of Schmidt and Thannhauser (*7*), served as the starting material for the analysis of desoxyribose nucleic acid (DNA) and total nucleic acid (*7, 8*). Ribose nucleic acid (RNA) was obtained by subtraction. The DNA and RNA values, in terms of milligrams of phosphorus per 100 g of fresh tissue, with Fisher *t* values, are given in Table 1. Succinic dehydrogenase contents, expressed as the conventional Q_{O_2}, together with body-weight data are entered in Table 2. In no case were the livers pooled. Only values for the individual samples were averaged. Analysis of variance applied to the succinic dehydrogenase results showed significance only in the comparison of controls and irradiated animals of group C (48 hours after treatment, significant at the 1-percent level).

Table 1. Nucleic acid content of liver from control and x-irradiated animals (sacrificed on the second and fifth days after treatment).*

Treatment	No. of animals†	DNAP‡	RNAP‡
Group A			
Controls§	12	17.68±0.69	66.88±5.11
Irradiated (2 days)	10	21.38±4.35	64.57±5.83
Irradiated (5 days)	10	17.00±0.60	75.62±3.53

* The standard error (S.E.) follows each ± sign.
† The respective body weights (g ± S.E.) of the control rats and those sacrificed 2 days and 5 days after irradiation were 270.5 ± 5.5, 262.3 ± 6.4, and 263.4 ± 4.0 at surgery and 260.6 ± 5.4, 253.2 ± 7.3, and 250.8 ± 5.0 at necropsy.
‡ Milligrams of P per 100 g fresh liver. Fisher *t* values for the comparison of controls with the 2-day and 5-day treatment series were 1.89 and 0.73 (DNAP) and 0.29 and 1.36 (RNAP), in the order given ($P > 0.05$).
§ Average value for controls, groups of six that were sacrificed on the second and fifth days after sham surgery.

Table 2. Succinic dehydrogenase levels of control and x-irradiated rat liver.*

Treatment	Post-treatment (days)	No. of animals†	Succinic dehydrogenase activity, Q_{O_2}±S.E.‡
Group B			
Controls	1	10	94.92±3.93
Irradiated	1	10	94.27±4.54
Group C			
Controls	2	13	91.60±2.44
Irradiated	2	13	83.50±2.58
Group D			
Controls	5	13	93.33±3.85
Irradiated	5	12	93.64±3.78
Group E			
Controls	11	14	95.29±2.79
Irradiated	11	13	91.70±2.53
Group K			
Controls (0.50-percent cysteine diet)	2	14	89.22±4.78
Irradiated (0.50-percent cysteine diet)	2	15	86.41±2.22

* Except for group K, all rats received the control ration.
† Initial body weights (g ± S.E.) for rats of groups B, C, D, E, and K were 260.3 ± 5.6, 253.4 ± 2.2, 251.2 ± 3.1, 243.9 ± 3.2, and 286.1 ± 3.1, respectively. The corresponding values at necropsy were 270.7 ± 4.1, 239.5 ± 1.7, 238.5 ± 2.2, 258.6 ± 4.4, and 279.1 ± 2.9.
‡ A statistically significant difference was noted solely for group C (analysis of variance).

It will be noted that hepatic DNA and RNA values of rats 2 or 5 days after exposure to x-ray at a dosage of 6500 r did not differ significantly from the respective control values (Table 1). Although the differences between liver succinic dehydrogenase contents of irradiated animals that were sacrificed 1, 5, or 11 days after treatment and those contents for the corresponding controls were not statistically significant, a definite, though minimal, depression in enzyme activity was evident with the 48-hour series (group C, Table 2). Under the same conditions of irradiation and time, but with recourse to the 0.50-percent cysteine diet (group K), no decrease was observed. This might be indicative of a protective action exerted by cysteine on the sulfhydryl-dependent enzyme. As is shown in the tables, the average body-weight changes were quite small for all groups.

The aforementioned results are in marked contrast to those of Di Bella, who reported succinic dehydrogenase decreases of 30 percent or greater for liver removed 24 or 48 hours after x-irradiation at dosages of 600 r and 800 r (*9*). The enzyme activity remained unchanged 24 hours after treatment at 500 r, with only a slight decrease after 48 hours at a level of 500 r. Cysteine or glutathione failed to alleviate the enzyme inhibition (48 hours, 800 r). However, Di Bella's conditions comprised total body exposure of immature rats to filtered x-ray (maximal dosage, 800 r) rather than exposure of the liver alone. Although his results lack statistical rigor, such trends might derive indirectly from damage to more sensitive tissues.

The absence of any remarkable alterations in the succinic dehydrogenase and nucleic acid levels of irradiated intact liver, which are rather sensitive criteria for the evaluation of radiation involvement, indicates a relative radio-resistance for this organ under these conditions. This is further reflected in the gross and microscopic examination of the liver sections, none of which exhibited any noteworthy changes either in the cells or tissue architecture.

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References and Notes

1. This study was aided by a grant from the Toni Division of the Gillette Company. The authors are indebted to I. F. Hummon, director of the Radiation Center, and R. S. Landauer, Cook County Hospital, Chicago, Ill., for the x-ray facilities; to H. C. Pirkle, department of pathology, University of Louisville School of Medicine, Louisville, Ky., for his aid in the histological examination of slides; and to Ruth Zelman and Harry Domnas for technical assistance.
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23 January 1956

What is most needed for learning is an humble mind.—CONFUCIUS.

Book Reviews

Theories of Learning. Ernest R. Hilgard. Appleton-Century-Crofts, New York, ed. 2, 1956. 563 pp. Illus. $5.50.

Hilgard's revision merits more than the casual notice usually accorded a second edition of a standard textbook, for Hilgard's book stands almost alone as a guide to students of what has become in America the most actively explored field of experimental psychology. As it happens, the revision, while retaining its old form, represents a thorough reworking of the field, a complete rewriting of many chapters, the addition of much new material, and a bringing of the bibliography up to date. The first edition is still a valuable book, but the new one is indispensable.

"Learning theory" may be considered the typically American contribution to experimental psychology. Following Darwin and Pavlov, and guided by Dewey and Thorndike, psychologists in this country have been fascinated by the problem of explaining how man becomes molded by his environment into the person that he is. Broadly stated, this is the problem of "learning." American psychologists, in keeping with the Jeffersonian tradition, tend to seek a basis for the understanding of man in the laws that govern individual development. If all men are born equal, the explanation of their diversity must be referred to the influences of varying environments. In other words, men are what they are because of what they have learned. Can the natural laws of learning be formulated on the basis of observation and tested by logic and experiment? This has been the major preoccupation of American experimental psychology for more than half a century.

The literature on the theory of learning is enormous, and it bulges each year with hundreds of new titles, many of which represent utterly inconsequential contributions. Few psychologists have the time and patience to read it all, and fewer still have the scholarly perspective that will enable them to follow the trails of theory through the jungle of words. Hilgard gives us a steer. He identifies theories, presents the evidence for each with impeccable fairness, and leaves us (almost) free to draw our own conclusions.

For the readers of *Science*, most of whom are not psychologists, Hilgard's book can be recommended as a good introduction to experimental psychology, far better than any of the introductory textbooks that we impose on our students. Hilgard does not pretend to present all of psychology, but he gives us a wise and scholarly appraisal of one of psychology's most important fields. He knows his subject, knows how to communicate his enthusiasm, and—unusual among psychologists—knows how to use the English language.

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Précis de gérontologie. Léon Binet and François Bourlière. Masson, Paris, 1955. vii + 554 pp. Illus. Paper, F. 3800; cloth, 4500.

It is virtually impossible to squeeze a review of even so young a discipline as gerontology into 554 pages. The authors have not attempted this feat but have placed upon a clearly presented background of gerontology (the science of aging) an up-to-date compendium of modern medical thinking and practice dealing with older people (geriatrics).

The first impression of an awe-inspiring reference work is replaced on closer acquaintance with the attractiveness of a readable and stimulating review. The interesting and varied presentation can be attributed, in part, to a long list of competent collaborators.

The first five chapters constitute the gerontological background for the volume. In Chapter 1, Binet and Bourlière give a good summary of the status of the general biological problems of aging. In Chapter 2, Pacaud presents the psychological aspects of gerontology, and in Chapter 5, Daric gives a demographic summary of aging in France and discusses its socio-economic consequences. Chapter 3 on "Age and infection" and Chapter 4 on "Cancer and Gerontology" complete this part of the book, which covers just 105 pages.

The authors indicate that the next 12 chapters "study successively the physiology and pathology of each of the organs and functions of the human body." The chapters on the blood, arteriosclerosis, the respiratory apparatus, the digestive system, the kidney, and the endocrine glands fulfill this intent by achieving a good balance between the biological and clinical aspects of the discussions. The chapters on the heart, the prostate gland, the musculoskeletal system, the skin, the sense organs, and the nervous system are, however, more clinical in presentation and do not provide much physiological background. The book is concluded by Chapter 18 on "Gerontologic surgery" and Chapter 19 on "Therapeutic aspects of the aging problem."

This handsomely bound volume is printed on good paper with large readable type. The photographs, among 184 figures, are especially well reproduced. The bibliographies, which appear at the end of each chapter, range from a complete list of references following Chapter 1 to no references following Chapter 18. The authors recognize the limitation of their bibliography and refer the reader to N. W. Shock's *A Classified Bibliography of Gerontology and Geriatrics.* The somewhat topical subject index is strongly supplemented by a table of contents that includes the page numbers of the chapter subheads.

The title and the authors' statements indicate that the book is designed to aid the student and the physician who is interested in gerontology. It should be especially helpful to the physician to have, in one volume, some background of gerontology and a complete geriatric review. The authors have succeeded in filling the literary space between the more definitive works on gerontology and the more specifically geriatric works. They have provided an international type of summary by drawing heavily on the American and English literature. This book should be helpful to anyone who is interested in the problems of aging.

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Einführung in die Geometrie der Waben. vol. IV, *Elemente der Mathematik vom Höheren Standpunkt aus.* Wilhelm Blaschke. Birkhäuser, Basel-Stuttgart, 1955. 108 pp. Illus. DM. 15.25.

An encyclopedic book on the same subject by Blaschke, one of the principal workers in the field, and G. Bol appeared in 1938 under the title *Geometrie der Gewebe.* According to the preface, *Gewebe* (web or textile fabric) was changed to *Wabe* (honeycomb) because the author prefers being associated with apiarists rather than weavers.

Either term has little connection with

the strictly mathematical concept of web. For the benefit of the noninitiated: The simplest type consists of three one-parameter families of curves in the plane (or a part of it) such that through every point there is exactly one curve of each family. If each of the families consists of parallel lines, hexagons may be constructed as follows: consider a triangle ca_1a_2 whose sides belong to the three families, construct a_3 as the intersection of the parallels to a_1a_2 through c and to ca_1 through a_2. Proceed in the same way with the triangle ca_2a_3 obtaining a_4, and so forth. Then $a_7 = a_1$. This construction is possible in other webs, but in general $a_7 \neq a_1$. If always $a_7 = a_1$ the web is called hexagonal. A typical problem is the characterization of the hexagonal webs and the definition of a measure (called curvature) for the local deviation of an arbitrary web from a hexagonal one.

This book is no mere excerpt from the older work; the methods are thoroughly different, based on Pfaffian forms and exterior differentiation. This permits the author to cover a large territory in few pages. The four chapters deal with webs in the plane, webs of surfaces in space (consisting of four one-parameter families of surfaces), plane webs consisting of four one-parameter families of curves, and webs of curves in space. The connections with algebraic geometry are particularly intriguing—for instance, rectilinear hexagonal webs consist of the tangents of a curve of class three.

Calculations, as opposed to synthetic reasonings, play a greater part in this book than in its predecessor; at times the author himself seems to regret this tendency, for instance (p. 64) where he speaks of creating a little geometric light in a wild forest of formulas. Nevertheless, the book is very readable and transparent and can be recommended as an excellent introduction to the subject. Because in his other works the author often disturbs the reader by extraneous—that is, nonmathematical—prejudices, I emphasize that this little book is not open to such objections.

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Physiology of Digestion. I. P. Pavlov. Academy of Medical Sciences of the U.S.S.R., Moscow, 1952. 508 pp. (In Russian).

This is an elegant and complete collection of all of Pavlov's publications in the field of the physiology of digestion. It includes the famous lecture series, all of Pavlov's papers on his ingenious surgical and experimental techniques, as well as a great number of articles previously scattered in various journals. The surgical papers contain numerous neat and clear-cut drawings, which every physiologist and surgeon would greatly appreciate. This volume also includes six of Pavlov's erudite essays on the broad general principles of the physiology of digestion, with particular reference to clinical problems and applications. One of these papers represents the presentation made by Pavlov at Stockholm in 1904 on the occasion of his acceptance of the Nobel prize.

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Lectures on Theoretical Physics. vol. V, *Thermodynamics and Statistical Mechanics.* Arnold Sommerfeld. F. Bopp and J. Meixner, Eds. Translated by J. Kestin, Academic Press, New York, 1956. 401 pp. $7.

Sommerfeld has compiled the lectures that he gave to his students into six volumes. The present volume completes the series on theoretical physics and deals with thermodynamics, kinetic theory, and statistical mechanics. Unfortunately Sommerfeld died before he had finished the manuscript of this volume, and it has been completed and edited by J. Bopp and J. Meixner.

The first three chapters and part of the fourth had been virtually completed by the author. The subject matter of the latter part of Chapter IV had been discussed with the editors, but the presentation and method are theirs. Sommerfeld had not decided on the contents of Chapter V, which is entirely the work of the editors, although the sections on the electron theory of metals are based on the well-known article by Sommerfeld and Bethe in the *Handbuch der Physik*.

Chapter I develops the general considerations of thermodynamics. Thermodynamics had a very practical origin, and the author stresses the technical aspect of the subject. Sommerfeld avoids any notation, such as dx, for nonperfect differentials, preferring to think in terms of *properties* of systems and their associated perfect differentials. In this light, the main importance of the second law of thermodynamics (which is discussed here by the methods of both Clausius and Caratheodory) is that it shows the existence of a property (the entropy) of a system and shows that under certain well-defined conditions the entropy never decreases. The chapter concludes with a section on the origin and consequences of the Nernst heat theorem.

Chapter II applies the results of Chapter I to special systems, such as dilute solutions and galvanic cells. The section on black-body radiation follows the original train of thought by which Planck arrived at his radiation law. It is a feature of this book that, without ever disturbing the logical development of the subject, the historical approach is discussed whenever possible and the presentation is extremely clear and readable.

Chapter III, on elementary kinetic theory, gives an introduction to statistical mechanics. The statistical significance of the van der Waals constants and the classical derivation of the Langevin function amplify the earlier sections on these subjects. Statistical fluctuations are exemplified in the very elegant section on Brownian motion.

In Chapter IV classical statistical mechanics is developed by Boltzmann's enumeration method, and the ensemble theory of Gibbs is only mentioned. Quantum statistics are introduced by the Darwin-Fowler method, whereas the combinatorial method would have been more in keeping with the general tone of the book as an undergraduate textbook.

Chapter V, which deals with the Maxwell-Boltzmann transport equation and its solution by the method of moments, is at a much higher level of difficulty, and the editors are forced to refer the reader more often to specialized papers.

At the end of the book there is an excellent collection of questions appropriate to the subject matter of the various chapters and some 40 pages of comment and hints for solution.

The translator has succeeded in preserving the clarity and elegance of presentation of the original, and this volume is to be highly recommended to teachers and students of classical thermodynamics and statistical mechanics.

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Protoplasmatologia. Handbuch der Protoplasmaforschung. vol. XI. *Protoplasmatische Pflanzenanatomie.* Lotte Reuter. Springer, Vienna, 1955. 131 pp. Illus. $8.10.

Workers in the fields of experimental plant anatomy and developmental physiology will appreciate Lotte Reuter's monograph, which correlates the extensive studies in "protoplasmic anatomy" by Friedl Weber and his school with parallel or related trends in dynamic anatomy elsewhere. Although not all the aspects and reports dealing with structure, development, physiological state and function, and differentiation are covered completely, a satisfactory synthesis of main results in the chosen fields has been obtained.

The first part of the book deals with

methodology; there are three headings: cell-physiological trends; cytomorphological trends, and correlative effects. The cell-physiological methods comprise the determination of conditions and changes at the level of chemical and colloidal events, such as viscosity, osmotic value, permeability, vital staining, isoelectric point, and differences in resistance to chemical or physical attack between cells and tissues. Methods designed for the study of cytomorphological data deal with observations at the level of microscopic order in cytoplasm, nucleus, plastids, chondriosomes, vacuole, and other cell constituents. Correlative effects are chiefly defined as gradients, polarity phenomena, and intercellular patterns.

The results and the present state of protoplasmic anatomy are outlined in the second part of the book, which includes (i) discussions on metabolism, development, and polarity in the living cell, (ii) many histological data arranged under the headings of the Haberlandtian tissue systems, and (iii) a section dealing with organs such as algal thalli, mycelia, and prothalli and with the general body of mosses, ferns, and flowering plants. A brief discussion of some aspects of normal and abnormal development and of regeneration concludes the volume, the usefulness of which is increased by illustrations, bibliographies after each subject, and author and plant name indexes.

One certainly cannot lay aside this small monograph without being reminded of the fact that experiment and physiological criteria are now extensively used in anatomical research. Often the difference between protoplasmic anatomy and cellular physiology appears to be one of definition rather than of methodology. The overlapping of research fields and methods, a characteristic of present-day science, is now very evident in plant anatomical work.

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Principles of Renal Physiology. Homer W. Smith. Oxford University Press, New York, 1956. 237 pp. Illus. $5.

This book is to some extent an abridgment of Homer Smith's more extensive monograph entitled *The Kidney, Structure and Function in Health and Disease,* published in 1951. Thus, the first third of the book treats classical renal morphology, theories of renal function, and principles of measurement of glomerular filtration rate, renal blood flow, tubular reabsorption, and tubular secretion. In the chapters devoted to these latter topics, specific mechanisms are described for reabsorption of glucose, amino acids, urea, protein, and so forth, and for secretion of para-amino hippuric acid, diodrast, and phenol red. Such problems as competitive interference and self-depression of tubular transport are briefly, though lucidly, discussed.

The second third of the book is devoted to the regulation of the water and salt composition of the body. The treatment of excretion and tubular reabsorption of water and strong electrolytes is classically "Smithian." Osmolar clearance and free water clearance, concepts that trouble even renal physiologists, are simply explained. The treatment of acid-base regulation, including acid excretion and bicarbonate reabsorption, is typically "Pittsian."

The last third of the book, made up of a series of appendixes, is an extension of scope rather than an abridgment of the longer treatise. Appendix I is a moderately detailed, rather one-sided discussion of electron microscopy of the kidney. Appendix II deals with, but will scarcely serve to popularize, the Henderson-Hasselbalch equation. Other sections describe chemical and mechanical procedures involved in clearance determinations. The bibliography is selective.

A number of the chapters of the book are closed by problems and questions. I frequently found it necessary to look up the answers in the "pony"; hence, I would not recommend lifting these questions *in toto* for the examination of other than first-quality students. Medical students, practitioners, graduate students, and investigators, in fact anyone with a passing interest in the kidney, will find something of value in this book. For those of us in the bifocal age, the typography is not all that might be desired. However, a reasonable price and jacket-pocket size excuse this transgression.

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New Books

The Genus Achlya: Morphology and Taxonomy. University of Michigan Studies, Scientific Series vol. XX. Terry W. Johnson, Jr. University of Michigan Press, Ann Arbor; Geoffrey Cumberlege, Oxford University Press, London, 1956. 180 pp. $4.50.

Synthetic Ion-Exchangers. Recent developments in theory and application. G. H. Osborn. Macmillan, New York, 1956. 194 pp. $6.

Organic Chemistry. Louis F. Fieser and Mary Fieser. Reinhold, New York, ed. 3, 1956. 1112 pp. $10.

Solid State Physics. vol. II, *Advances in Research and Applications.* Frederick Seitz and David Turnbull, Eds. Academic Press, New York, 1956. 468 pp. $10.

Animal Nutrition. Leonard A. Maynard and John K. Loosli. McGraw-Hill, New York, 1956. 484 pp. $7.50.

Miscellaneous Publications

(Inquiries concerning these publications should be addressed, not to Science, *but to the publisher or agency sponsoring the publication.)*

Report of an International Conference on Operator Theory and Group Representations. 20–23 Oct. 1953, Arden House, Harriman, N.Y. Publ. 387. National Academy of Sciences–National Research Council, Washington, D.C., 1955. 37 pp.

Inventory and Price List of Electromagnetically Enriched and Other Stable Isotopes. Stable Isotopes Research and Production Div., Oak Ridge National Laboratory, Oak Ridge, Tenn., 1956. 17 pp.

Ohio State University, Health Physics Conference. 13–15 June 1955. Columbus, Ohio. Office of Radiation Safety, Ohio State University, Columbus; U.S. Atomic Energy Commission, Washington, D.C., 1956. 223 pp.

The Baccalaureate Origins of the Science Doctorates Awarded in the United States from 1936 to 1950 Inclusive. National Academy of Science–National Research Council, Washington, 1955. 158 pp. $2.

Composting. Sanitary disposal and reclamation of organic wastes. Harold B. Gotaas. WHO Monogr. Ser. No. 31. World Health Organization, Geneva, 1956. 205 pp. $5.

A Decade of Research: 1946–1956. Cornell Aeronautical Laboratory, Inc. of Cornell University, Buffalo 21, N.Y., 1956. 66 pp.

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Meetings and Societies

Scientific Basis of Weather Modification

Shortly after the 1946 discovery of the Dry-Ice cloud seeding technique by Schaefer (Schenectady) and during the first rush of amateur and commercial rain makers who were showering a bewildered public with a variety of claims of success for turning supercooled clouds into precipitating snow and rain, a whimsical but unknowingly pertinent cartoon appeared in a national magazine. It showed two clergymen quizzically gazing through a church window at the raindrops spattering outside, with one asking the other, "I wonder if its theirs or ours?" Ten years later, the clergyman's problem is still very much the meteorologist's problem, but the latter is steadily narrowing the range of his uncertainty. In the course of his efforts to so delimit his uncertainty, the meteorologist has virtually developed a whole new branch of his field, cloud physics, and the past decade's effort to learn useful techniques of modifying clouds has entrained the services of chemists, physicists, statisticians, and even astronomers.

In an attempt to take stock of the present position of cloud modification and related fields, an international Conference on the Scientific Basis of Weather Modification Studies was held 10–12 Apr. at the University of Arizona's Institute of Atmospheric Physics. This conference brought together at one time and in one place scientists representing nearly every one of the world's leading cloud modification research groups. Nine foreign scientists (whose travel to the conference was supported through a grant from the Rockefeller Foundation) and 26 U.S. scientists presented research results on all aspects of the problem, ranging from the physics and chemistry of nucleation through the seeding of large cyclonic storms and on into the intricacies of statistical evaluation of seeding results.

If a discerning layman had come to this conference with a primary interest in the question of whether scientists had yet found a practicable way of increasing precipitation, his conclusion after listening to their papers and discussions for 3 days would have to be that, as yet, whatever successes they have are confined to certain very favorable situations. In contrast to the often glowing claims that have emanated in recent years from some commercial cloud-seeders, the observer would have heard from this gathering of researchers a long series of still unsettled questions that bear crucially on the techniques and economics of artificial cloud nucleation.

The only indications of substantial positive results from the usual commercial-type seeding operations, using ground-based silver iodide generators, for which present statistical significance was claimed at the conference were the results of an evaluation made by the staff of President Eisenhower's Advisory Committee on Weather Control. The evaluations dealt with a number of commercial rain-making operations carried out in selected winter storms in the mountainous West Coast region during the past few years. These evaluations were subjected to rather strong criticisms by some of the statisticians present, on the basis that it was not possible to draw valid conclusions from this type of operation owing to lack of randomization in the tests, and secondarily because of certain possible errors in the statistical model used in the analysis (a point that did not become quite clear to nonstatisticians present but whose resolution appears to be in sight).

It was pointed out, however, by Thom (Washington), who supervised the evaluations, that the Advisory Committee for Weather Control had been required, by virtue of its statutory obligations, to use such data, and had sought to extract therefrom what statistical information it could, notwithstanding the lack of scientific design in the original operations. He urged that the positive indications obtained should be considered primarily as suggesting further research on the seeding potentialities in the areas studied.

The difficulties encountered by the advisory committee in carrying out its responsibilities were generally recognized by the conferees; however, there was the feeling expressed that because of these technical statistical uncertainties, some implications of recent committee communications and press statements may not have been warranted. This question hinges in part on statistical questions that are still to be settled. All other conference reports of scientific efforts to appraise the effects of past cloud-seeding efforts seemed to fall into one or the other of the following categories: (i) experiments on a small scale (on individual clouds or cloud groups) in which some indisputable positive effects have been observed; (ii) large-scale experiments which have not so far yielded clearly established positive results of recognized significance, either because the technique used was inefficient or because the sensitivity of the statistical tests employed was low owing to lack of adequate observational data.

Notwithstanding the fact that no dramatic research results on rain-making techniques were reported, an observer would have found in the proceedings of this conference a number of indications of cautious optimism on the part of the scientists regarding *future* developments and could have seen clearly that the decade of research which was being reviewed had brought real progress in the form of greatly increased knowledge of the physics of clouds and precipitation. It seemed agreed that recent progress has been nowhere more significant than in the recognition, just within the past few years, that the growth of raindrops by collision and coalescence is as important as the classical ice-crystal process for natural precipitation. And one cloud-seeding technique in particular, that directed at dissipating stratus cloud decks, seemed to be accepted as an accomplished fact, based especially on work summarized by aufm Kampe and Weickmann (Belmar).

Optimism was expressed by many conferees relative to the prospects of inducing significant increases of precipitation under certain restricted types of weather conditions in regions where a broad air current is forced to rise over an extensive mountain barrier. Under such conditions, clouds tend to form more or less continually and, equally important, strong air currents are present to transport into the clouds seeding agents (notably silver iodide particles) released from ground generators. Conference attention seemed to center on such mountain-barrier regions, chiefly because recent experiments in several parts of the world have cast certain doubts on the extent to which ground-released nuclei reach cloud altitudes over any other types of terrain before photolytic decay or surface changes deactivate the nuclei, although much more work is still required on these questions. Ludlam (London and Stockholm) mentioned forthcoming tests to be made under essentially these mountain-barrier conditions in Sweden. Bowen (Sydney) described seeding experiments now in progress, wherein aircraft are releasing silver iodide in a randomized time sequence at cloud altitudes upwind from

the Snowy Mountains in southeastern Australia. In the latter case, the first year's results showed substantial positive effects, but Bowen emphasized the lack of statistical significance at this stage.

Neumann (Tel Aviv) reported seeding trials that have been underway in Israel for 3 years but have not been well known in this country. Seeding with ground-based silver iodide generators is conducted on a randomized basis. The accumulated experience of the first 3 years' work suggested that something of the order of 50 years of such randomized trials would be needed to detect a 20-percent increase at the 5-percent confidence level using the original statistical design, so efforts are now being made to incorporate a more efficient design into the tests.

Braham, Battan, and Byers (Chicago) discussed several aspects of still another randomized seeding experiment in which aircraft released large amounts of water spray (drops of the order of 100 μ in diameter) into clouds over Puerto Rico and obtained statistically significant radar evidence that this treatment *initiated* precipitation processes in the tradewind clouds. Rough calculations suggest economic difficulties in consequence of the inherently high expense of flying thousands of gallons of water to cloud-top altitudes. This experiment, nevertheless, stands out as the first in which a clear-cut positive effect of cloud seeding has been demonstrated in a carefully designed randomized treatment scheme.

There has long been recognition that existing methods of generating silver iodide (*e.g.*, burning acetone solutions of silver iodide) may be very far from optimal. However, uncomfortably little truly careful work to examine the generator processes and output has been done in the past decade. It was, therefore, most encouraging to hear Mason (London) report current studies wherein electron diffraction and x-ray diffraction techniques are being used to study the nature of the particles produced by several basic methods. Mason reported that almost none of them contained the simple hexagonal (icelike) crystalline silver iodide, as had always been assumed, but rather that mixed crystals, often of cubic lattice, predominated. Mason believes that their poor crystalline structure is a result of reduction of AgI to metallic silver under the influence of the hydrogen present in the combustion atmosphere of generators. His findings document the need for intensive study of nuclei generators and hold out, implicitly, hope that research could yield marked improvements in this phase of seeding technology. Sänger (Zürich) reported interesting evidence that he has recently found which suggests that cupric sulfide may be equal in effectiveness to silver iodide as an ice-nucleating material and less subject to decay effects.

A number of papers on many of the more detailed problems now confronting cloud-modification research added greatly to the success of the conference, but they will not be summarized here, since they are of somewhat less general interest. The proceedings of the conference are being published in the form of a collection of mimeographed 500- to 1000-word summaries of the papers presented. A limited number of copies will be available to educational and research institutions in this country and abroad. Requests should be addressed to the Institute of Atmospheric Physics, University of Arizona, Tucson.

It seemed to me that this conference did fulfill very well its intended purpose of taking stock of the present status of research in cloud modification and cloud physics. From it, the conclusion may be drawn that the past decade of effort counsels greater conservatism regarding the extent to which clouds may be made to yield precipitation than was initially manifested by enthusiastic exponents of seeding. The present seeding techniques may fall short of producing increases that can easily be identified, the number of situations in which real effectiveness of seeding potentially exists may be more limited than originally hoped, or the large natural variability of precipitation may be obscuring statistical discrimination of even substantial increases. Perhaps all three of these factors play a part in the still existing uncertainty regarding the efficacy of man's most recent rain-making efforts. This still leaves room for what Reichelderfer (Washington) described in his conference paper as "realistic optimism," a term in which the adjective connotes due respect for the many complexities of the natural processes that occur within clouds and the noun connotes a feeling that we cannot possibly have optimized seeding techniques yet and much remains to be learned.

In all, there was quite complete agreement among the conferees that a strong case can be made for still more vigorous cloud-modification and cloud-physics research. A considerable measure of agreement was reached at the conference concerning the chief lines along which such research might best be directed in the near future.

JAMES E. MCDONALD
Institute of Atmospheric Physics, University of Arizona, Tucson

Meeting Notes

■ An international symposium on particle accelerators, detection techniques and high-energy physics, which was arranged by the European Organization for Nuclear Research, was held 11–22 June at the Institut de Physique in Geneva, Switzerland. The following countries were represented at the conference: Australia, Belgium, Canada, Czechoslovakia, Denmark, France, Federal Republic of Germany, Greece, India, Italy, Japan, Netherlands, Norway, Spain, Sweden, Switzerland, U.S.S.R., United Kingdom, U.S.A., and Yugoslavia. UNESCO also sent an observer.

The first week of the symposium was devoted entirely to high-energy particle accelerators. During that period, about 50 papers were given on the chief problems raised by the construction of modern accelerators, such as the theoretical aspects of the question, the study of magnets, the radio-frequency accelerating system, the injection and ejection of particles, the operation of the machines, and so forth. The technical features of the large accelerators now in operation or being built were explained in detail, and finally, entirely new principles were put forward whose practical application would considerably improve the performance of existing accelerators.

During the second week of the symposium, attention was focussed on detection methods and on the theoretical aspects and experimental techniques of the physics of elementary particles. The 70 papers delivered dealt with a wide variety of questions, such as Wilson chambers, bubble chambers, over-compression and counting techniques, experimental and theoretical physics concerning mesons, nucleons and antiprotons, quantum field theories, the structure of the proton, mesic atoms, and so forth. A news report from Geneva states that the exchanges of views that took place between participants, both inside and outside the conference room, proved extremely fruitful, and that the frankness shown by all concerned bodes well for the possibility of future international cooperation in physics.

■ The 28th meeting of the Pan American Sanitary Organization Executive Committee ended on 13 June with the signing of its final report embodying 16 resolutions. The meeting opened on 5 June under the chairmanship of Jorge Jiménez Gandica, director of the Division of Public Health of Colombia. Manuel A. Sanchez Vigil, director of the National Institute of Hygiene, Nicaragua, was vice-chairman. Most of the resolutions adopted will be presented for final action to the PASO Directing Council at its ninth meeting, which is scheduled to convene on 16 Sept. in Antigua, Guatemala.

The $2,400,000 budget proposed by Fred L. Soper, director of the Pan American Sanitary Bureau, Regional Office of the World Health Organization, for the bureau's operations in 1957 was ap-

proved by the committee. This represents an increase of $200,000 over the 1956 budget.

Looking toward construction within the next few years of new offices more suitable for the expanding operations of the bureau, the committee approved the director's recommendation to add $100,000 surplus funds to a Building Reserve Fund, bringing that fund up to $200,000. A recommendation that $23,524 be used to meet initial architectural expenses for the new building also was approved.

The committee has asked the directing council to authorize the director to draw on the Building Reserve Fund "in the event that additional funds should be necessary for the intensification of the malaria eradication program." Throughout the session great stress was laid on the program for the eradication of malaria throughout the Americas, a program which has been made worldwide by the World Health Organization and which might require additional funds to meet any critical situation that might arise.

■ Within the past year the American Academy of Microbiology has been established and incorporated in the State of Delaware. The organization was formed to: (i) promote the highest professional standing of microbiologists, (ii) carry on professional activities on behalf of the science of microbiology, and (iii) promote programs of recognition, certification and/or accreditation of microbiologists where needed to accomplish the aforesaid purposes.

A board of governors has been named to organize and administer the affairs of the academy and receive applications for fellowship. Fellows in the academy will be required to have a doctor's degree, or a level of education which is acceptable to the committee on election and the board of governors, and a minimum of 7 years of postdoctoral work in microbiology. The members of the board of governors are J. H. Bailey, I. L. Baldwin, W. J. Cromartie, G. M. Dack, S. R. Damon, R. Donovick, G. Edsall, H. O. Halvorson, R. D. Housewright, P. W. Kabler, R. G. E. Murray, E. H. Spaulding, R. A. Starkey, J. T. Syverton, and Orville Wyss. The executive secretary is G. I. Wallace, and the present office of the academy is 456 Noyes Laboratory, Urbana, Ill.

■ The Thomas Alva Edison Foundation was host to the National Committee for the Development of Scientists and Engineers at a 1-day conference at West Orange, N.J., on 21 June. The purpose of the conference was to present to a group of representative citizens a discussion of the factors in our national life that generate the unusual demands for highly qualified scientific and technical personnel. The conference was open to the press. On the following day, the National Committee held its second regular meetings in executive session (the President established the committee on 3 Apr.).

The opening session was addressed briefly by Charles Edison, honorary president of the Thomas Alva Edison Foundation; Howard L. Bevis, chairman of the National Committee and president of Ohio State University; and Charles F. Kettering, president of the Edison Foundation and former vice-president of General Motors. The chief addresses on the morning program were given by Clifford Furnas, assistant secretary of the Department of Defense, who discussed the "Requirements growing out of the nation's security needs"; and Herbert Scoville, Jr., assistant director of the Central Intelligence Agency, who spoke on "Maintaining America's technological superiority—the threat of Russian competition."

Lee A. DuBridge, president of California Institute of Technology, addressed the afternoon session on the "Special need for highly qualified scientific and technological personnel," and M. H. Trytten, director of the Office of Scientific Personnel, National Academy of Sciences–National Research Council, delivered an "Assessment of the general trends in the supply of scientific and engineering manpower."

At the dinner meeting two groups of case studies on the current and potential shortages of technical manpower were presented. Charles B. Jolliffe, vice president and technical director of the Radio Corporation of America, described the situation in the electronics industry, and George W. Best, director of chemical research for the Ethyl Corporation, discussed the situation in chemistry.

■ A working party of senior geologists concerned with the preparation of a regional geological map for Asia and the Far East recently concluded a 5-day meeting in Bangkok under the chairmanship of V. P. Sondhi (India). This was the second session of the working party, which included some 50 participants from 13 countries and territories, among them the directors of geological surveys in Burma, China, India, Indonesia, Japan, the Republic of Korea, Malaya, and Thailand and specialists from France, the Netherlands, the U.S.S.R., the United States, and Hong Kong. The meeeting was held under the sponsorship of the Economic Commission for Asia and the Far East.

Major decisions reached included plans for financing the preparation of the map; questions of coordination of various national works; target date for completion of country geological maps; map projection; and preparation of index maps showing the status of geological surveys. The meeting also decided to begin compilation of a regional mineral distribution map for Asia and the Far East, as well as regional maps showing mineralization epochs and provinces as a guide for mineral prospecting. An *ad hoc* committee composed of India, Indonesia, and Japan was established to assist in this work.

■ Data on safeguards associated with the types of research and power reactors being developed by the United States and the United Kingdom were exchanged at a joint meeting held in Chicago, 12–15 June, under the terms of the U.S.-U.K. Agreement for Cooperation. Classified papers were included in the agenda and attendance was limited primarily to representatives of the United Kingdom and of the U.S. Atomic Energy Commission. U.S. papers will be made available to interested U.S. industrial concerns under the Access Permit Program.

A second reactor safety meeting on U.S. problems, open to "L" and "Q"-cleared employees of access permit holders, will be held in the late fall or early winter. It is hoped that access permit holders will submit papers and suggest topics to be included on the program for the second meeting.

■ The 61st summer meeting and the 36th colloquium of the American Mathematical Society will be held at the University of Washington, 20–25 Aug. The meetings are in conjunction with the meetings of the Biometric Society, the Econometric Society, the Institute of Mathematical Statistics, and the Mathematical Association of America.

Salomon Bochner of Princeton University will deliver the colloquium lectures, entitled "Harmonic analysis and probability." C. B. Allendoerfer of the University of Washington will present a 1-hour address on "Some recent advances in differential geometry in the large," and Kenkichi Iwasawa of the Massachusetts Institute of Technology, will speak for an hour on "A theorem on Abelian groups and its application in algebraic number theory." There will be a session of invited 20-minute papers in applied mathematics. For information, write to the American Mathematical Society, 80 Waterman St., Providence 6, R.I.

■ The 15th International Congress of Pure and Applied Chemistry (analytical chemistry) will be held in Lisbon, Portugal, 9–16 Sept. under the sponsorship of the International Union of Pure and Applied Chemistry. According to the provisional program, the scientific sessions will include five general lectures, ten sub-section lectures, and individual papers limited to 10–20 minutes.

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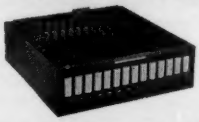

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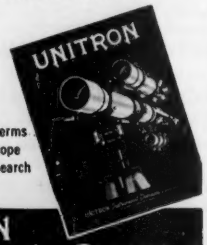

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are as follows: microchemical methods; biological methods; electrical methods; optical methods; radio chemical methods; organic complexes; results and statistical interpretations; methods of absorption and distribution; generalities and standardization of methods and different applications.

Excursions are being planned for the congress participants, including possibly a 4-day voyage to the Island of Madeira. In addition to a series of social events, the organizing committee is arranging visits to various factories in the Lisbon area.

The president of the National Academy of Sciences–National Research Council has appointed the following U.S. representatives to the congress: S. E. Q. Ashley, General Electric Company; Roger G. Bates, National Bureau of Standards; W. D. Cooke, Cornell University; G. M. Kline, National Bureau of Standards; I. M. Kolthoff, University of Minnesota; Walter J. Murphy, American Chemical Society; F. D. Tuemmler, Shell Development Company; John Turkevich, Princeton University; Grant T. Wernimont, Eastman Kodak Company; Philip W. West, Louisiana State University; and John H. Yoe, University of Virginia.

■ The U.S. National Committee of the International Scientific Radio Union has scheduled a meeting at the University of California, Berkeley, 11–12 Oct. A combined technical session of interest to all participants will be held on the morning of 11 Oct., to be followed by one or more sessions in each of the following fields: Commission 2, radio and troposphere; Commission 3, ionospheric radio; and Commission 4, radio noise of terrestrial origin.

Authors are invited to submit titles and 100 to 200 word abstracts *before 20 July*. The abstracts should be sent to the appropriate commission chairman or secretary: Commission 2, Dr. J. B. Smyth, Smyth Research Associates, 3930 Fourth Ave., San Diego 3, Calif.; Commission 3, Prof. L. A. Manning, Stanford University, Stanford, Calif.; Commission 4, Prof. A. W. Sullivan, University of Florida, Gainesville, Fla.

Forthcoming Events

August

13–16. National Medical Assoc., 61st annual, New York, N.Y. (J. T. Givens, 1108 Church St., Norfolk 10, Va.)

15–22. Canadian Teachers' Federation, Fredericton, N.B., Canada. (G. G. Croskery, 444 MacLaren St., Ottawa, Ontario, Canada.)

16–21. Symposium on X-Ray Microscopy and Microradiography, Cambridge, England. (W. C. Nixon, Cavendish Lab., Cambridge.)

17–25. International Cong. of Entomology, 10th, Montreal, Canada. (J. A. Downes, Div. of Entomology, Science Service Bldg., Ottawa, Ont., Canada.)

19–23. International Cong. on Diseases of the Chest, 4th, Cologne, Germany. (Executive Offices, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Ill.)

19–24. International Symposium on Combustion, 6th, New Haven, Conn. (Combustion Symposium Office, Mason Lab., Yale Univ., New Haven 11.)

20–21. Mathematical Assoc. of America, 37th summer, Seattle, Wash. (H. M. Gehman, Univ. of Buffalo, Buffalo 14, N.Y.)

20–21. National Telemetering Conf., Los Angeles, Calif. (R. E. Rawlins, Lockheed Aircraft Corp., Burbank, Calif.)

20–24. Conf. on Scientific and Technical Writing, Philadelphia, Pa. (H. F. Arader, Univ. of Pennsylvania, 3400 Walnut St., Philadelphia 4.)

20–24. Institute of Mathematical Statistics, Seattle, Wash. (G. E. Nicholson, Jr., Dept. of Statistics, Univ. of North Carolina, Chapel Hill.)

20–24. International Cong. of Physical Medicine, 2nd, Copenhagen, Denmark. (S. Clemmesen, Kommune-hospitalet, Copenhagen.)

20–24. Plant Science Seminar, 33rd annual, St. Louis, Mo. (F. L. Mercer, St. Louis College of Pharmacy, St. Louis 10.)

20–25. American Mathematical Soc., 61st summer, Seattle, Wash. (J. H. Curtiss, AMS, 80 Waterman St., Providence 6, R.I.)

21–24. Western Electronic Show and Convention, Los Angeles, Calif. (B. Angwin, General Electric Co., 11840 W. Olympic Blvd., Los Angeles 64.)

22–29. World Cong. of Sociology, 3rd, Amsterdam, Netherlands. (T. B. Bottomore, Skepper House, 13 Endsleigh St., London, W.C.1, England.)

24–28. American Astronomical Soc., joint with Astronomical Soc. of the Pacific, Berkeley, Calif. (J. A. Hynek, Harvard College Observatory, Harvard Univ., Cambridge 38, Mass.)

26–30. American Inst. of Biological Sciences, Storrs, Conn. (H. T. Cox, 2000 P St., NW, Washington 6.)

The following 23 meetings are being held in conjunction with the AIBS meeting at Storrs, Conn.

26–30. American Bryological Soc. (L. J. Gier, Dept. of Biology, William Jewell College, Liberty, Mo.)

26–30. American Fern Soc., annual. (Mildred E. Faust, 501 University Pl., Syracuse 10, N.Y.)

26–30. American Microscopical Soc. (R. W. Pennak, Dept. of Biology, Univ. of Colorado, Boulder.)

26–30. American Soc. for Horticultural Science, annual. (F. S. Howlett, Ohio Agricultural Experimental Station, Wooster, Ohio.)

26–30. American Soc. of Human Genetics. (E. J. Gardner, Dept. of Zoology, Utah State Agricultural College, Logan.)

26–30. American Soc. of Limnology and Oceanography, annual. (B. H. Ketchum, Woods Hole Oceanographic Institution, Woods Hole, Mass.)

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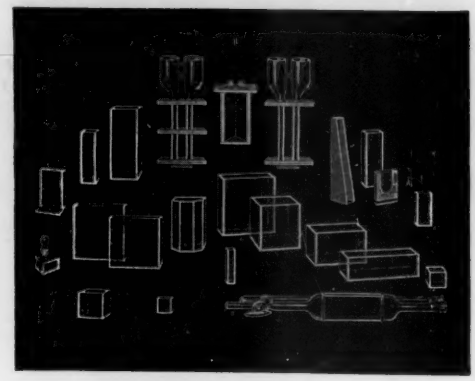

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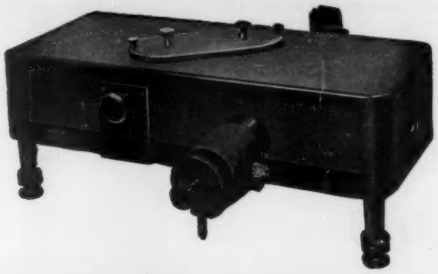

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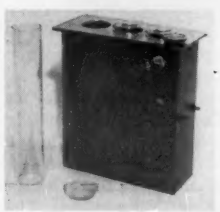

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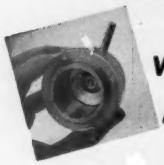

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26–1. International Soc. of Haematology, 6th cong., Boston, Mass. (ISH, New England Medical Center, Harrison Ave. at Bennet St., Boston 11.)

27–31. Biological Photographic Assoc., 26th annual, Rochester, N.Y. (BPA, c/o 343 State St., Rochester 4.)

27–31. Colloquium on Statistical Mechanics of Transport Processes, IUPAP, Brussels, Belgium. (I. Prigogine, 40 Avenue F. D. Roosevelt, Brussels.)

27–31. Infrared Spectroscopy Inst., 7th annual, Nashville, Tenn. (N. Fuson, Dept. of Physics, Fisk Univ., Nashville 8.)

28–2. Colloquium on Semiconductors and Phosphors, IUPAP, Garmisch-Partenkirchen, Germany. (H. Maier-Leibnitz, Walter-von-Dyck-Platz 1, Munich 2, Germany.)

29–5. British Assoc. for the Advancement of Science, annual, Sheffield, England. (Secretary, BAAS, Burlington House, Piccadilly, London, W.1., England.)

29–8. International Soc. of Soil Science, 6th cong., Paris. (F. A. Van Baren, ISSS, Royal Tropical Inst., Mauritskade 63, Amsterdam, Netherlands.)

30–5. American Psychological Assoc., Chicago, Ill. (F. H. Sanford, 1333 16 St., NW, Washington 6.)

30–5. Psychometric Soc., Chicago, Ill. (L. V. Jones, Dept. of Psychology, Univ. of Chicago, Chicago 37.)

September

1–9. International Cong. of Anthropological and Ethnological Sciences, 5th, Philadelphia, Pa. (Secretary, American Organizing Committee, International Cong. of Anthropology, National Acad. of Sciences–National Research Council, 2101 Constitution Ave., Washington 25.)

2–7. Laurentian Hormone Conf., AAAS, Mont Tremblant, Quebec, Canada. (Committee on Arrangements, LHC, 222 Maple Ave., Shrewsbury, Mass.)

4–5. Meteoritical Soc., 19th meeting, Bloomington, Ind. (C. W. Beck, Dept. of Geology, Indiana Univ., Bloomington.)

4–6. International Assoc. of Milk and Food Sanitarians, annual, Seattle, Wash. (H. L. Thomasson, IAMFS, Box 437, Shelbyville, Ind.)

(See issue of 15 June for comprehensive list)

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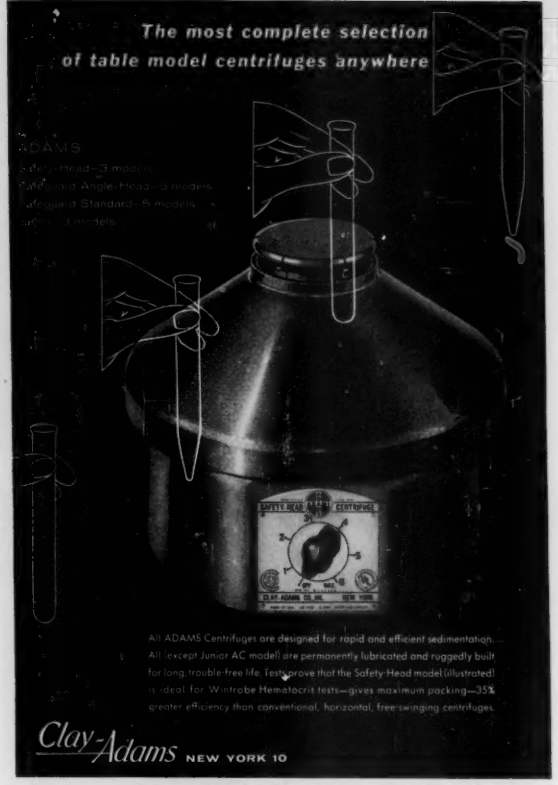

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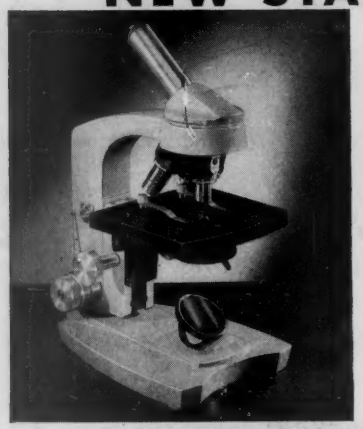
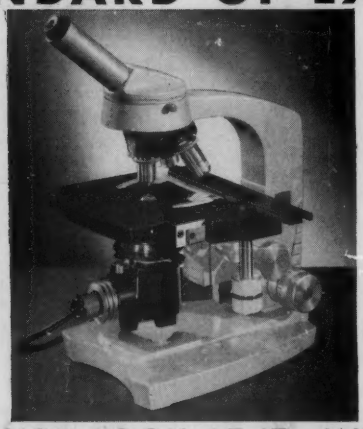
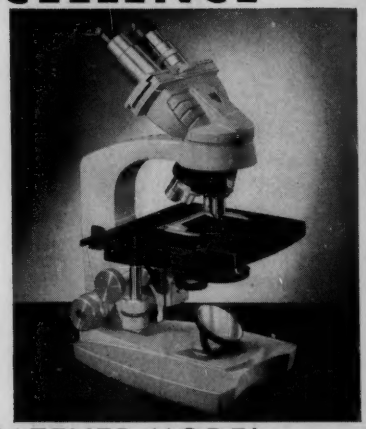

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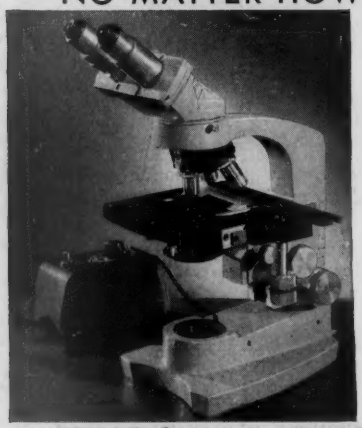
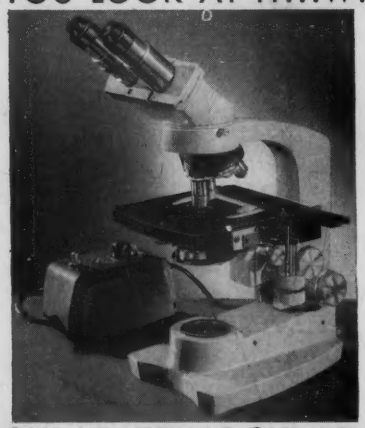
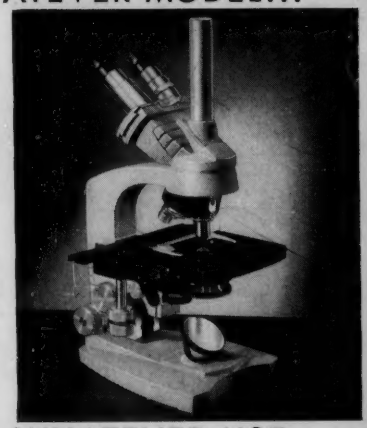

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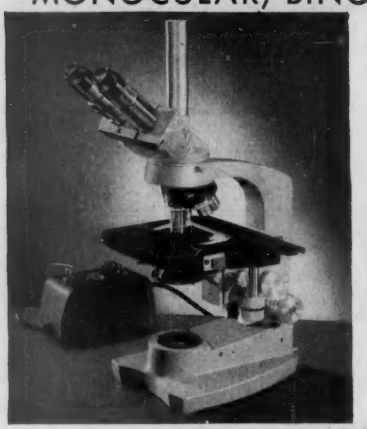
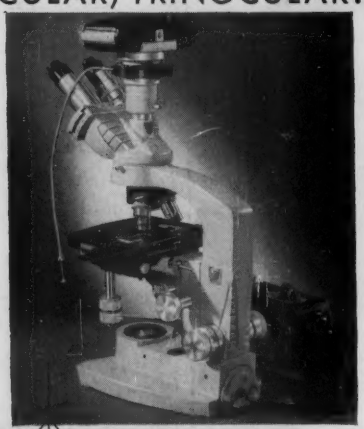
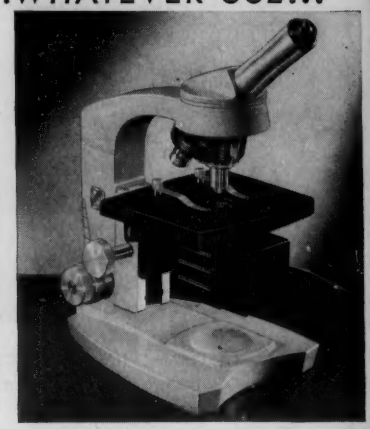

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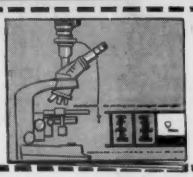

Dept. G-2

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